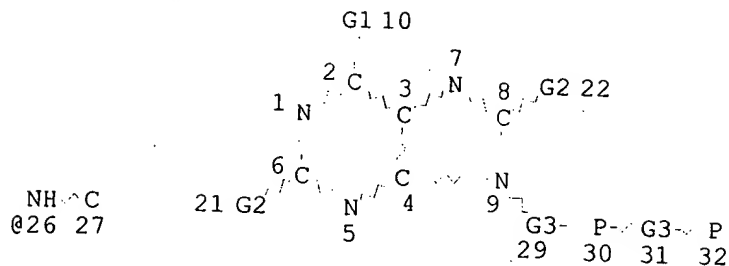


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Me N-C
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VAR G1=NH2/26/24
VAR G2=H/X/O/S/N/28
REP G3=(0-20) A
NODE ATTRIBUTES:
NSPEC IS RC AT -25
NSPEC IS RC AT 27
NSPEC IS RC AT 28
CONNECT IS E2 RC AT 1
CONNECT IS E2 RC AT 5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L11 166 SEA FILE=REGISTRY SSS FUL L9
L12 SCR 2017
L13 166 SEA FILE=REGISTRY SUB=L11 SSS FUL L12

FULL SUBSET SCREEN SEARCH COMPLETED
SEARCH TIME: 00.00.01

166 ANSWERS

L13 ANSWER 1 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 389121-36-2 REGISTRY
CN 5'-Thymidylic acid, 3'-azido-3'-deoxy-, monoanhydride with
[[(1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy]methyl]phosphonic acid
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H26 N10 O10 P2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16

Beuch

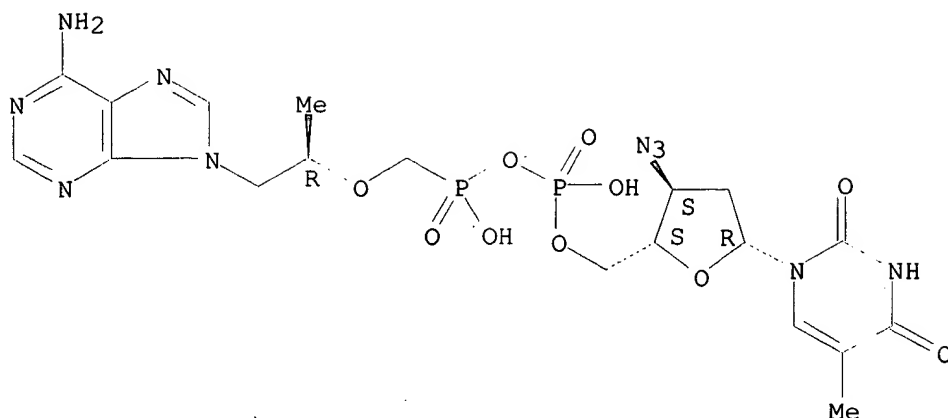
740653

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653

041

60



1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:95613 Inhibition of HIV-1 replication in macrophages by red blood cell-mediated delivery of a heterodinucleotide of azidothymidine and 9-(R)-2-(phosphono methoxypropyl)adenine. Franchetti, P.; Rossi, L.; Cappellacci, L.; Pasqualini, M.; Grifantini, M.; Balestra, E.; Forbici, F.; Perno, C-F.; Serafini, S.; Magnani, M. (Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, 62032, Italy). Antiviral Chemistry & Chemotherapy, 12(3), 151-159 (English) 2001. CODEN: ACCHEH. ISSN: 0956-3202. Publisher: International Medical Press.

AB Monocyte-derived macrophages (M/M) are considered important in vivo reservoirs for different kinds of viruses, including HIV. Hence, therapeutic strategies are urgently needed to protect these cells from virus infection or to control viral replication. In this paper, we report the synthesis, target delivery and in vitro efficacy of a new heterodinucleotide (AZTpPMPA), able to inhibit HIV-1 prodn. in human macrophages. AZTpPMPA consists of two established anti-HIV drugs [zidovudine (AZT) and tenofovir (PMPA)] chem. coupled together by a phosphate bridge. This drug is not able to prevent p24 prodn. when administered for 18 h to M/M exptl. infected with HIV-1 Bal (inhibition 27%), but can almost completely suppress virus prodn. when given encapsulated into autologous erythrocytes (inhibition of p24 prodn. 97%). AZTpPMPA is slowly converted to PMPA, AZT monophosphate and AZT (36 h half-life at 37.degree.) by cell-resident enzymes. Thus AZTpPMPA should be considered a new prodrug of AZT and PMPA that is able to provide stoichiometric amts. of both nucleoside analogs to macrophage cells and to overcome the low phosphorylating activity of M/M for AZT and the modest permeability of PMPA.

L13 ANSWER 2 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 370588-67-3 REGISTRY

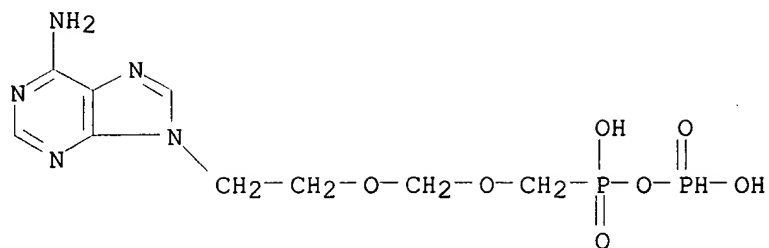
CN Diphosphonic acid, [[[2-(6-amino-9H-purin-9-yl)ethoxy]methoxy]methyl]-(9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C9 H15 N5 O7 P2

SR CA

LC STN Files: CA, CAPLUS



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:331633 Synthesis of .beta.-H-phosphono-.alpha.-phosphonomethyl analogues of nucleoside 5'-diphosphates. Ivanov, A. V.; Jasko, M. V.; Alexandrova, L. A. (Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, 119991, Russia). Russian Journal of Bioorganic Chemistry (Translation of Bioorganicheskaya Khimiya), 27(4), 264-266 (English) 2001. CODEN: RJCET. ISSN: 1068-1620. Publisher: MAIK Nauka/Interperiodica.

AB Novel .beta.-H-phosphono-.alpha.-phosphonomethyl analogs of nucleoside 5'-diphosphates were synthesized by phosphorylation of 5'-O-phosphonomethylthymidine and 9-[(2-phosphonomethoxy)ethyl]adenine with sodium pyrophosphate. The structures of the resulting individual compds. were confirmed by NMR and UV spectroscopy.

L13 ANSWER 3 OF 166 REGISTRY COPYRIGHT 2002 ACS

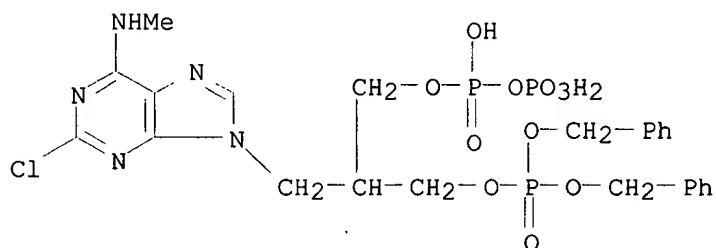
RN 369627-08-7 REGISTRY

CN Diphosphoric acid, mono[3-[[bis(phenylmethoxy)phosphinyl]oxy]-2-[[2-chloro-6-(methylamino)-9H-purin-9-yl]methyl]propyl] ester, ammonium salt (9CI) (CA INDEX NAME)

MF C24 H29 Cl N5 O11 P3 . x H3 N

SR CA

LC STN Files: CA, CAPLUS



● x NH3

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:331630 Acyclic and Cyclopropyl Analogues of Adenosine Bisphosphate Antagonists of the P2Y1 Receptor: Structure-Activity Relationships and Receptor Docking. Kim, Hak Sung; Barak, Dov; Harden, T. Kendall; Boyer, Jose L.; Jacobson, Kenneth A. (Molecular Recognition Section Laboratory of Bioorganic Chemistry, National Institute of Diabetes Digestive and Kidney Diseases National Institutes of Health, Bethesda, MD,

20892-0810, USA). Journal of Medicinal Chemistry, 44(19), 3092-3108 (English) 2001. CODEN: JMCMAR. ISSN: 0022-2623. Publisher: American Chemical Society.

AB The activation of P2Y1 receptors in platelets contributes to platelet aggregation, and selective antagonists are sought as potential antithrombotic agents. The authors reported (Kim et al. J. Med. Chem. 2000, 43, 746-755) that acyclic analogs of adenine nucleotides, contg. two phosphate groups on a sym. branched aliph. chain, attached at the 9-position of adenine, are moderately potent P2Y1 receptor antagonists. In this study they have varied the chain structure to include asym. substitution, olefinic, and cyclopropyl groups. These antagonists inhibited the stimulation of phospholipase C in turkey erythrocyte membranes induced by 30 nM 2-MeS-ADP in the micromolar range. In the series of sym. branched aliph. groups substituted with two phosphate groups, the optimal antagonist potency occurred with the 2-methylpropyl group. A 2-chloro-N6-methyladenine deriv., 2-[2-(2-chloro-6-methylaminopurin-9-yl)methyl]propane-1,3-bisoxo(diammoniumphosphate), was a full antagonist at the P2Y1 receptor with an IC50 value of 0.48 .mu.M. Esterification of one of the phosphate groups or substitution with O-acetyl greatly reduced the antagonist potency at the P2Y1 receptor. Removal of a methylene group of 2-[2-(2-chloro-6-methylaminopurin-9-yl)methyl]propane-1,3-bisoxo(diammoniumphosphate) or inclusion of an olefinic or cyclopropyl group also reduced potency. A pair of enantiomeric glycerol derivs. demonstrated a 5-fold stereoselectivity for the S-isomer. Stereoisomerically defined analogs of 2-[2-(2-chloro-6-methylaminopurin-9-yl)methyl]propane-1,3-bisoxo(diammoniumphosphate) contg. a cyclopropyl group in place of the branched carbon were less potent as antagonists, with IC50 values of 2-3 .mu.M. No agonist activity was obsd. for these analogs. A new rhodopsin-based mol. model of the P2Y1 receptor indicated that the optimal docked orientation of the two monophosphate moieties relative to the adenine N6 (compared to a rigid, bicyclic analog) was consistent with the dependence of antagonist potency on chain length. The 3'-phosphate was predicted to occupy a restricted space, deeper in the binding cleft than the 5'-phosphate location. In summary, modification of the flexible spacer chain linking bisphosphate groups to the adenine moiety provided many moderately potent antagonists.

L13 ANSWER 4 OF 166 REGISTRY COPYRIGHT 2002 ACS

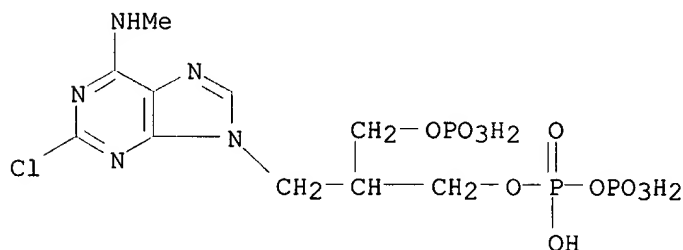
RN 369626-81-3 REGISTRY

CN Diphosphoric acid, mono[2-[[2-chloro-6-(methylamino)-9H-purin-9-yl)methyl]-3-(phosphonooxy)propyl] ester, ammonium salt (9CI) (CA INDEX NAME)

MF C10 H17 Cl N5 O11 P3 . x H3 N

SR CA

LC STN Files: CA, CAPLUS



x NH₃

1 REFERENCES IN FILE CA (1967 TO DATE)

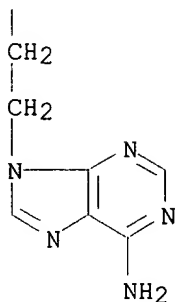
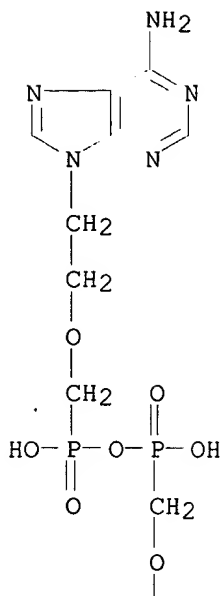
Searched by: Mary Hale 308-4258 CM-1 12D16

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:331630 Acyclic and Cyclopropyl Analogues of Adenosine Bisphosphate Antagonists of the P2Y1 Receptor: Structure-Activity Relationships and Receptor Docking. Kim, Hak Sung; Barak, Dov; Harden, T. Kendall; Boyer, Jose L.; Jacobson, Kenneth A. (Molecular Recognition Section Laboratory of Bioorganic Chemistry, National Institute of Diabetes Digestive and Kidney Diseases National Institutes of Health, Bethesda, MD, 20892-0810, USA). Journal of Medicinal Chemistry, 44(19), 3092-3108 (English) 2001. CODEN: JMCMAR. ISSN: 0022-2623. Publisher: American Chemical Society.

AB The activation of P2Y1 receptors in platelets contributes to platelet aggregation, and selective antagonists are sought as potential antithrombotic agents. The authors reported (Kim et al. J. Med. Chem. 2000, 43, 746-755) that acyclic analogs of adenine nucleotides, contg. two phosphate groups on a sym. branched aliph. chain, attached at the 9-position of adenine, are moderately potent P2Y1 receptor antagonists. In this study they have varied the chain structure to include asym. substitution, olefinic, and cyclopropyl groups. These antagonists inhibited the stimulation of phospholipase C in turkey erythrocyte membranes induced by 30 nM 2-MeS-ADP in the micromolar range. In the series of sym. branched aliph. groups substituted with two phosphate groups, the optimal antagonist potency occurred with the 2-methylpropyl group. A 2-chloro-N6-methyladenine deriv., 2-[2-(2-chloro-6-methylaminopurin-9-yl)methyl]propane-1,3-bisoxo(diammoniumphosphate), was a full antagonist at the P2Y1 receptor with an IC50 value of 0.48 .mu.M. Esterification of one of the phosphate groups or substitution with O-acetyl greatly reduced the antagonist potency at the P2Y1 receptor. Removal of a methylene group of 2-[2-(2-chloro-6-methylaminopurin-9-yl)methyl]propane-1,3-bisoxo(diammoniumphosphate) or inclusion of an olefinic or cyclopropyl group also reduced potency. A pair of enantiomeric glycerol derivs. demonstrated a 5-fold stereoselectivity for the S-isomer. Stereoisomerically defined analogs of 2-[2-(2-chloro-6-methylaminopurin-9-yl)methyl]propane-1,3-bisoxo(diammoniumphosphate) contg. a cyclopropyl group in place of the branched carbon were less potent as antagonists, with IC50 values of 2-3 .mu.M. No agonist activity was obsd. for these analogs. A new rhodopsin-based mol. model of the P2Y1 receptor indicated that the optimal docked orientation of the two monophosphate moieties relative to the adenine N6 (compared to a rigid, bicyclic analog) was consistent with the dependence of antagonist potency on chain length. The 3'-phosphate was predicted to occupy a restricted space, deeper in the binding cleft than the 5'-phosphate location. In summary, modification of the flexible spacer chain linking bisphosphate groups to the adenine moiety provided many moderately potent antagonists.

L13 ANSWER 5 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 368430-79-9 REGISTRY
 CN Diphosphonic acid, bis[[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]- (9CI)
 (CA INDEX NAME)
 FS 3D CONCORD
 MF C16 H22 N10 O7 P2
 SR CA
 LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

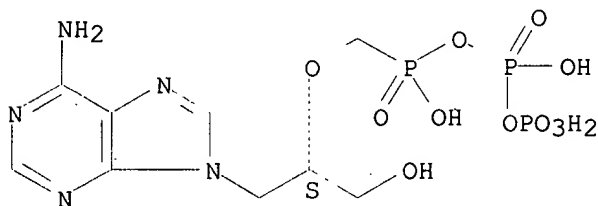
REFERENCE 1: 135:313179 Erythrocyte-mediated delivery of a new homodinucleotide active against human immunodeficiency virus and herpes simplex virus. Rossi, Luigia; Serafini, Sonja; Cappellacci, Loredana; Balestra, Emanuela; Brandi, Giorgio; Schiavano, Giuditta F.; Franchetti, Palmarisa; Grifantini, Mario; Perno, Carlo-Federico; Magnani, Mauro (Institute of Biochemistry "G. Fornaini", University of Urbino, Urbino, 61029, Italy). Journal of Antimicrobial Chemotherapy, 47(6), 819-827 (English) 2001. CODEN: JACHDX. ISSN: 0305-7453. Publisher: Oxford University Press.

AB Monocyte-derived macrophages (MDMs) play a central role in the pathogenesis of infection by human immunodeficiency virus (HIV-1) and

represent one of the main reservoirs of the virus in the body. In addn., MDMs can easily be infected by various herpes viruses, including herpes simplex virus type 1 (HSV-1). We have synthesized a new antiviral agent (Bis-PMEA) that consists of two 9-(2-phosphonylmethoxyethyl)adenine (PMEA) mols. bound by a phosphate bridge. This nucleotide analog, like the parent compd. PMEA, has strong and selective activity against HIV-1 and HSV-1. A drug-targeting system previously developed in our lab. was used for the selective delivery of these drugs of macrophages. Bis-PMEA and PMEA were encapsulated into autologous erythrocytes by a procedure of hypotonic dialysis and isotonic resealing. Loaded erythrocytes were modified to increase their recognition and phagocytosis by human macrophages. By administering Bis-PMEA-loaded erythrocytes to macrophages, 47% of Bis-PMEA and 28% of PMEA was still present 10 days after phagocytosis; in contrast, only 12% of PMEA was found in macrophages receiving PMEA-loaded erythrocytes. Bis-PMEA-loaded erythrocytes were then added to macrophages infected with HIV-1 and HSV-1 and their antiviral activity evaluated. Remarkable protection was obtained against HIV-1 and HSV-1 infection (95 and 85%, resp.). Therefore, Bis-PMEA acts as an efficient antiviral prodrug that, following selective targeting to macrophages by loaded erythrocytes, can protect a refractory cell compartment.

L13 ANSWER 6 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 352525-58-7 REGISTRY
 CN Diphosphoric acid, monoanhydride with [[(1S)-2-(6-amino-9H-purin-9-yl)-1-(hydroxymethyl)ethoxy]methyl]phosphonic acid trisodium salt, (S)- (9CI)
 (CA INDEX NAME)
 FS STEREOSEARCH
 MF C9 H16 N5 O11 P3 . 3 Na
 SR CA
 LC STN Files: CA, CAPLUS
 CRN (111964-44-4)

Absolute stereochemistry.



● 3 Na

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:153062 An alternative synthesis of HPMPC and HPMPA diphosphoryl derivatives. Otmar, Miroslav; Masojfdkova, Milena; Votruba, Ivan; Holy, Antonin (Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague, 166 10/6, Czech Rep.). Collection of Czechoslovak Chemical Communications, 66(3), 500-506 (English) 2001. CODEN: CCCCAK. ISSN: 0010-0765. Publisher: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic.
 AB In (S)-1-[3-hydroxy-2-(phosphonomethoxy)propyl]cytosine (HPMPC) and (S)-9-[3-hydroxy-2-(phosphonomethoxy)propyl]adenine (HPMPA) with 3-hydroxy

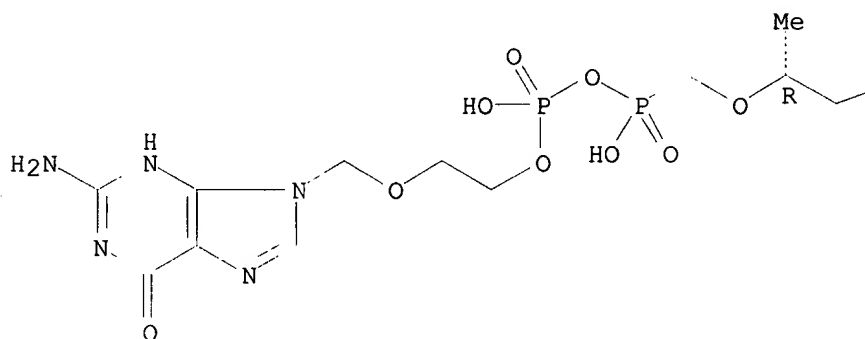
Searched by: Mary Hale 308-4258 CM-1 12D16

functions protected with 4,4'-dimethoxytrityl (DMTr) groups, phosphonate groups were transformed to the morpholides and treated with bis(tributylammonium) diphosphate. Selective cleavage of the DMTr group in the presence of the labile diphosphate residue was achieved in water at pH 2.5. Purifn. by charcoal adsorption followed by anion exchange chromatog. afforded phosphonate-diphosphate compds. (HPMPCpp, HPMPApp).

L13 ANSWER 7 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 308367-96-6 REGISTRY
 CN Isohypophosphoric acid, [[(1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy)methyl]-, P-[2-[(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)methoxy]ethyl] ester, diammonium salt (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C17 H24 N10 O9 P2 . 2 H3 N
 SR CA
 LC STN Files: CA, CAPLUS
 CRN (238411-89-7)

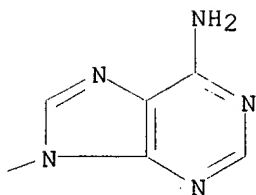
Absolute stereochemistry.

PAGE 1-A



● 2 NH3

PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:197 A new acyclic heterodinucleotide active against Human Immunodeficiency Virus and Herpes Simplex Virus. Franchetti, P.; Abu Sheikha, G.; Cappellacci, L.; Marchetti, S.; Grifantini, M.; Balestra, E.;

Searched by: Mary Hale 308-4258 CM-1 12D16

Perno, C.-F.; Benatti, U.; Brandi, G.; Rossi, L.; Magnani, M.
(Dipartimento di Scienze Chimiche, Università di Camerino, Camerino,
62032, Italy). Antiviral Research, 47(3), 149-158 (English) 2000. CODEN:
ARSRDR. ISSN: 0166-3542. Publisher: Elsevier Science B.V..

AB The most common therapies against human herpes virus (HSV-1) and human immunodeficiency virus (HIV-1) infectivity are based on the administration of nucleoside analogs. Acyclovir (ACV) is the drug of choice against HSV-1 infection, while the acyclic nucleoside phosphonate analog PMPA has shown marked anti-HIV activity in a phase I and II clin. studies. As monocyte-derived macrophages are assumed to be important as reservoirs of both HSV-1 and HIV-1 infection, new approaches able to inhibit replication of both viruses in macrophages should be welcome. ACVpPMPA, a new heterodinucleotide consisting of both an antiherpetic and an antiretroviral drug bound by a phosphate bridge, was synthesized and encapsulated into autologous erythrocytes modified to increase their phagocytosis by human macrophages. ACVpPMPA-loaded erythrocytes provided an effective in vitro protection against both HSV-1 and HIV-1 replication in human macrophages.

L13 ANSWER 8 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 278611-52-2 REGISTRY

CN Diphosphoric acid, monoanhydride with [[(1S)-2-(6-amino-9H-purin-9-yl)-1-[[bis(4-methoxyphenyl)phenylmethoxy)methyl]ethoxy)methyl]phosphonic acid (9CI) (CA INDEX NAME)

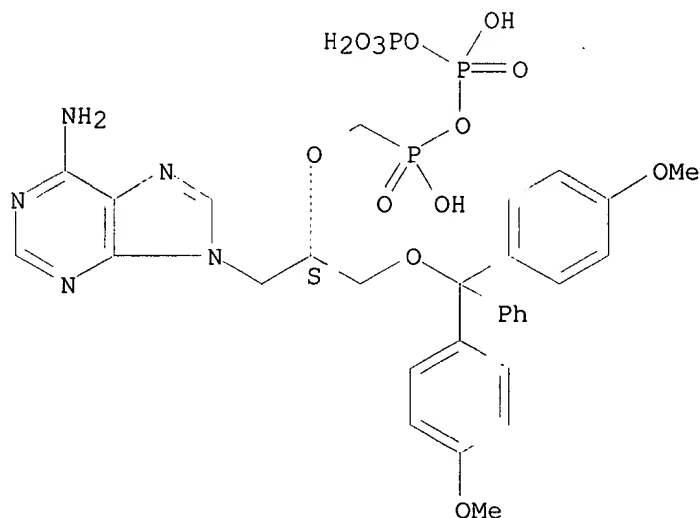
FS STEREOSEARCH

MF C30 H34 N5 O13 P3

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:153062 An alternative synthesis of HPMPA and HPMPA diphosphoryl derivatives. Otmar, Miroslav; Masojfdkova, Milena; Votruba, Ivan; Holy, Antonin (Institute of Organic Chemistry and Biochemistry,

Searched by: Mary Hale 308-4258 CM-1 12D16

Academy of Sciences of the Czech Republic, Prague, 166 10/6, Czech Rep.).
Collection of Czechoslovak Chemical Communications, 66(3), 500-506
(English) 2001. CODEN: CCCCAK. ISSN: 0010-0765. Publisher: Institute of
Organic Chemistry and Biochemistry, Academy of Sciences of the Czech
Republic.

AB In (S)-1-[3-hydroxy-2-(phosphonomethoxy)propyl]cytosine (HPMPC) and
(S)-9-[3-hydroxy-2-(phosphonomethoxy)propyl]adenine (HPMPA) with 3-hydroxy
functions protected with 4,4'-dimethoxytrityl (DMTr) groups, phosphonate
groups were transformed to the morpholides and treated with
bis(tributylammonium) diphosphate. Selective cleavage of the DMTr group
in the presence of the labile diphosphate residue was achieved in water at
pH 2.5. Purifn. by charcoal adsorption followed by anion exchange
chromatog. afforded phosphonate-diphosphate compds. (HPMPCpp, HPMPApp).

REFERENCE 2: 133:73888 An alternative synthesis of HPMPC and HPMPA
diphosphoryl derivatives. Otmar, Miroslav; Votruba, Ivan; Holy, Antonin
(Institute of Organic Chemistry and Biochemistry, Academy of Sciences of
the Czech Republic, Prague, 166 10, Czech Rep.). Collection Symposium
Series, 2(Chemistry of Nucleic Acid Components), 252-254 (English) 1999.
CODEN: CSYSFN. Publisher: Institute of Organic Chemistry and
Biochemistry, Academy of Sciences of the Czech Republic.

AB A symposium report. The authors have synthesized the triphosphonate of
(S)-1-(3-hydroxy-2-phosphonomethoxypropyl)cytosine via a morpholidate
activated intermediate using dimethoxytrityl as a hydroxy-protecting
group.

L13 ANSWER 9 OF 166 REGISTRY COPYRIGHT 2002 ACS

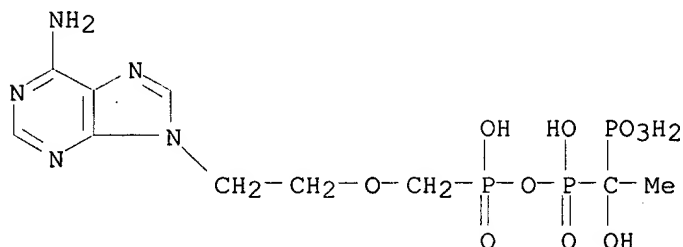
RN 255835-66-6 REGISTRY

CN Diphosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl](1-hydroxy-1-
phosphonoethyl)-, tetralithium salt (9CI) (CA INDEX NAME)

MF C10 H18 N5 O10 P3 . 4 Li

SR CA

LC STN Files: CA, CAPLUS



● 4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)

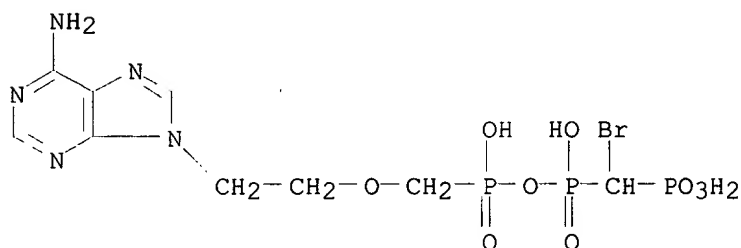
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside
phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.;
Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of
Physiology and Biophysics, Health Sciences Center, State University of New
York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry,
274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258.
Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs
with broad spectrum antiviral activity, were evaluated for potential

cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 10 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 255835-65-5 REGISTRY
 CN Diphosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy]methyl](bromophosphon
 omethyl)-, tetralithium salt (9CI) (CA INDEX NAME)
 MF C9 H15 Br N5 O9 P3 . 4 Li
 SR CA
 LC STN Files: CA, CAPLUS



● 4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

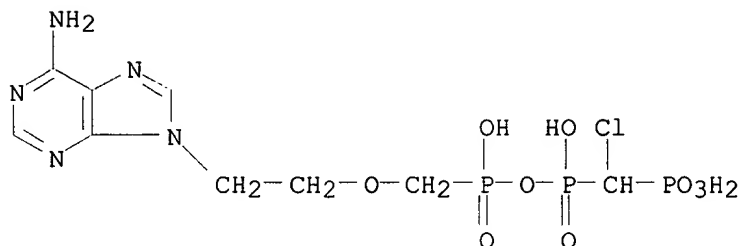
REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.; Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry, 274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs with broad spectrum antiviral activity, were evaluated for potential cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 11 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 255835-64-4 REGISTRY

Searched by: Mary Hale 308-4258 CM-1 12D16

CN Diphosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl](chlorophospho
nomethyl)-, tetralithium salt (9CI) (CA INDEX NAME)
MF C9 H15 Cl N5 O9 P3 . 4 Li
SR CA
LC STN Files: CA, CAPLUS



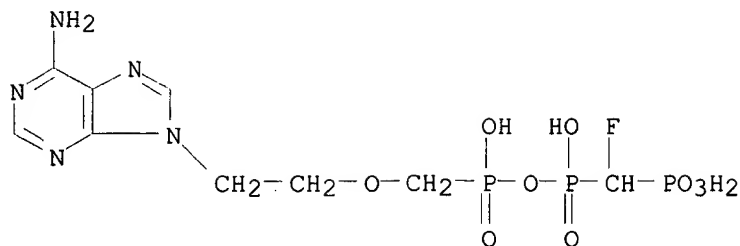
● 4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.; Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry, 274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs with broad spectrum antiviral activity, were evaluated for potential cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 12 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 255835-63-3 REGISTRY
CN Diphosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl](fluorophospho
nomethyl)-, tetralithium salt (9CI) (CA INDEX NAME)
MF C9 H15 F N5 O9 P3 . 4 Li
SR CA
LC STN Files: CA, CAPLUS



● 4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.; Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry, 274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs with broad spectrum antiviral activity, were evaluated for potential cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 13 OF 166 REGISTRY COPYRIGHT 2002 ACS

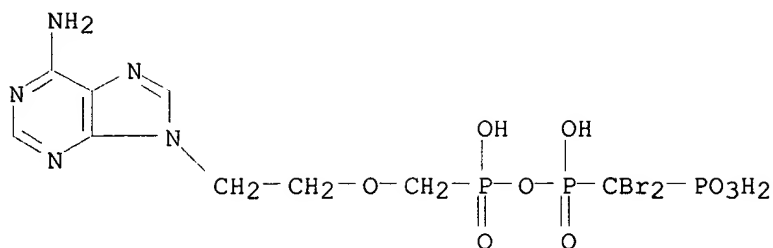
RN 255835-62-2 REGISTRY

CN Diphosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy]methyl] (dibromophosphonomethyl)-, tetralithium salt (9CI) (CA INDEX NAME)

MF C9 H14 Br2 N5 O9 P3 . 4 Li

SR CA

LC STN Files: CA, CAPLUS



● 4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.; Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry, 274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs with broad spectrum antiviral activity, were evaluated for potential cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 14 OF 166 REGISTRY COPYRIGHT 2002 ACS

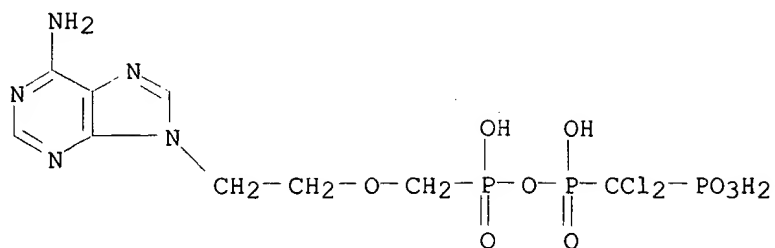
RN 255835-61-1 REGISTRY

CN Diphosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl](dichlorophosphonomethyl)-, tetralithium salt (9CI) (CA INDEX NAME)

MF C9 H14 Cl2 N5 O9 P3 . 4 Li

SR CA

LC STN Files: CA, CAPLUS



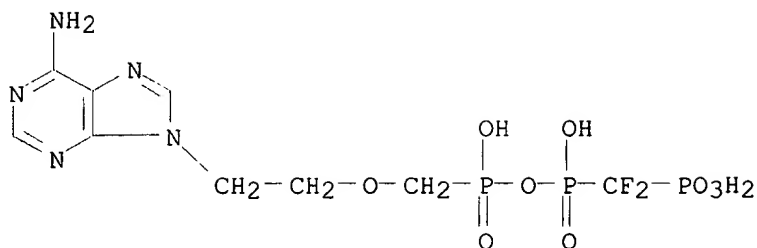
● 4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.; Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry, 274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs with broad spectrum antiviral activity, were evaluated for potential cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 15 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 255835-60-0 REGISTRY
CN Diphosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl](difluorophosphonomomethyl)-, tetralithium salt (9CI) (CA INDEX NAME)
MF C9 H14 F2 N5 O9 P3 . 4 Li
SR CA
LC STN Files: CA, CAPLUS



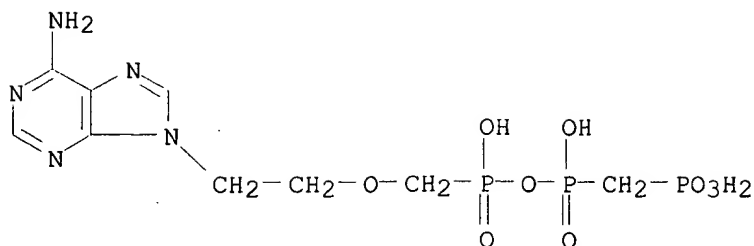
● 4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.; Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry, 274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs with broad spectrum antiviral activity, were evaluated for potential cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 16 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 255835-59-7 REGISTRY
CN Diphosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl](phosphonomethyl)-, tetralithium salt (9CI) (CA INDEX NAME)
MF C9 H16 N5 O9 P3 . 4 Li
SR CA
LC STN Files: CA, CAPLUS



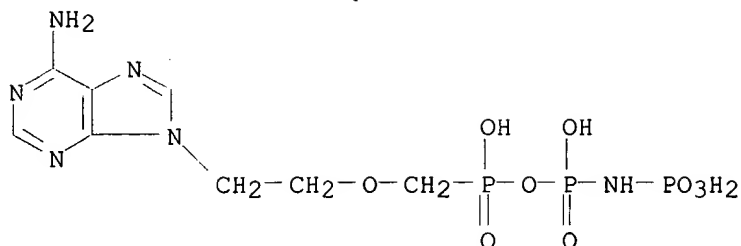
● 4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.; Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry, 274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs with broad spectrum antiviral activity, were evaluated for potential cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 17 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 255835-58-6 REGISTRY
CN Imidodiphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]phosphonic acid, tetralithium salt (9CI) (CA INDEX NAME)
MF C8 H15 N6 O9 P3 . 4 Li
SR CA
LC STN Files: CA, CAPLUS



● 4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.; Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry, 274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs with broad spectrum antiviral activity, were evaluated for potential cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 18 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 255835-57-5 REGISTRY

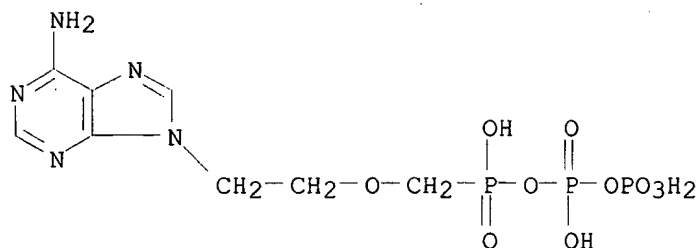
CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]phosphonic acid, tetralithium salt (9CI) (CA INDEX NAME)

MF C8 H14 N5 O10 P3 . 4 Li

SR CA

LC STN Files: CA, CAPLUS

CRN (129532-77-0)



●4 Li

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:102460 Inhibition of adenylyl cyclase by acyclic nucleoside phosphonate antiviral agents. Shoshani, Ilana; Laux, Wolfgang H. G.; Perigaud, Christian; Gosselin, Gilles; Johnson, Roger A. (Department of Physiology and Biophysics, Health Sciences Center, State University of New York, Stony Brook, NY, 11794-8661, USA). Journal of Biological Chemistry, 274(49), 34742-34744 (English) 1999. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Acyclic derivs. of adenine, known as highly effective nucleotide analogs with broad spectrum antiviral activity, were evaluated for potential cross-reactivity with adenylyl cyclases, a family of membrane-bound enzymes that share putative topologies at their catalytic sites with oligonucleotide polymerases and reverse transcriptases. A series of derivs. of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited a prepn. of adenylyl cyclase derived from rat brain with IC50 values that ranged from 66 .mu.M (PMEA) to 175 nM for its diphosphate deriv. (PMEApp) and mimics of it. PMEApp mimics included PMEAp(NH)p, PMEAp(CH2)p, PMEAp(CX2)p (X = fluorine, chlorine, or bromine), PMEAp(CHX)pp, and PMEAp(C(OH)CH3)pp. The data suggest that inhibition of adenylyl cyclases may contribute to the therapeutic action of some of these or similar compds. or constitute part of their side effects in therapeutic settings.

L13 ANSWER 19 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 238411-89-7 REGISTRY

CN Isohypophosphoric acid, [[(1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy)methyl]-, P-[2-[(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)methoxy]ethyl] ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

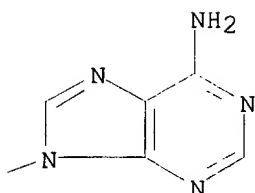
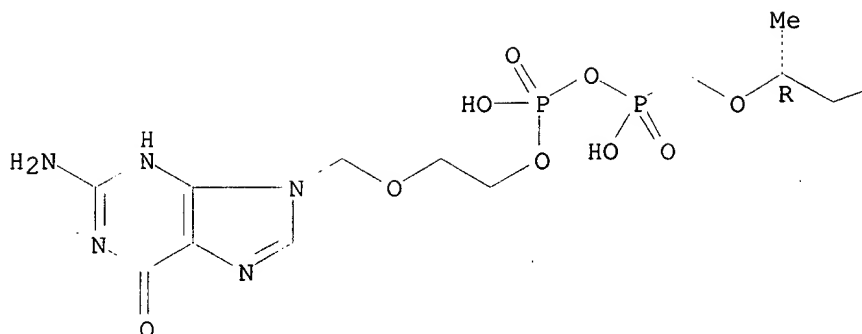
MF C17 H24 N10 O9 P2

CI COM

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:170563 Synthesis and biological application of a new heterodinucleotide with both anti-HSV and anti-HIV activity. Franchetti, Palmarisa; Sheikha, Ghassan Abu; Cappellacci, Loredana; Grifantini, Mario; Balestra, Emanuela; Perno, Carlo-Federico; Brandi, Giorgio; Rossi, Luigia; Magnani, Mauro (Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, 62032, Italy). Nucleosides & Nucleotides, 18(4 & 5), 989-990 (English) 1999. CODEN: NUNUD5. ISSN: 0732-8311. Publisher: Marcel Dekker, Inc..

AB A symposium reporting the synthesis of a new antiviral drug with both anti-HSV and anti-HIV activity by coupling Acyclovir and the acyclic nucleoside phosphonate (R)PMPA. The heterodinucleotide ACVpPMPA encapsulated into autologous erythrocytes was added to human macrophages providing an effective in vitro protection from HSV-1 and HIV-1 replication.

L13 ANSWER 20 OF 166 REGISTRY COPYRIGHT 2002 ACS

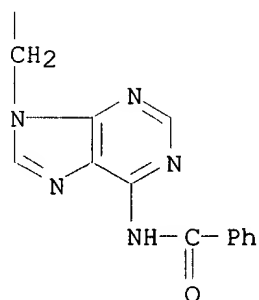
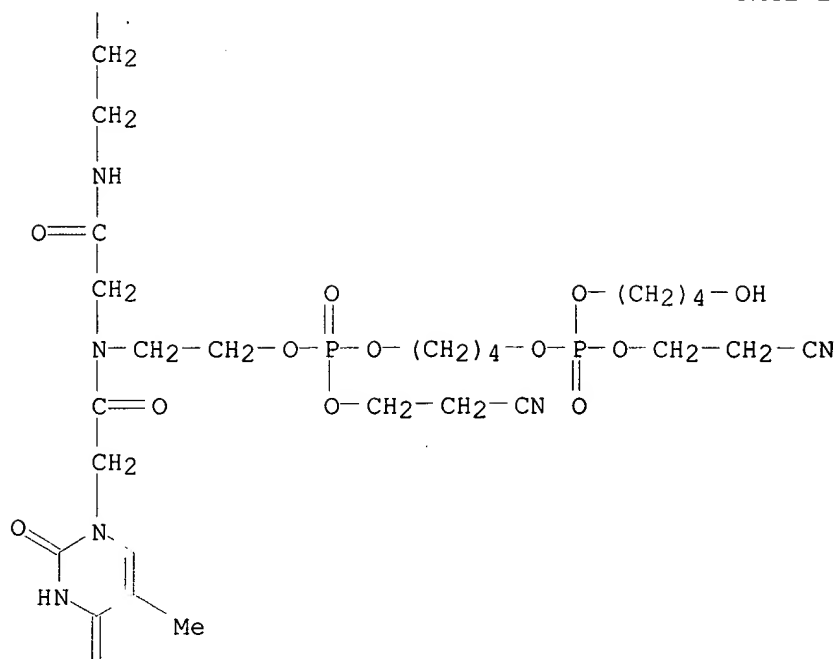
RN 225787-02-0 REGISTRY

CN Peptide nucleic acid, ((deamino)(hydroxy)T-bz6A-bz6A-bz6A-bz6A)-Gly-OH, (4-carboxyphenyl)methyl ester, 5'-[2-cyanoethyl 4-[[[(2-cyanoethoxy)(4-hydroxybutoxy)phosphinyl]oxy]butyl phosphate] (9CI) (CA INDEX NAME)

FS NUCLEIC ACID SEQUENCE

MF C107 H116 N34 O29 P2

SR CA

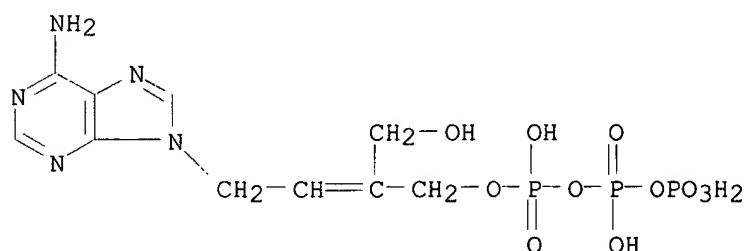


- 1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:19274 2',5'-oligoadenylate-peptide nucleic acids (2-5A-PNAs) activate RNase L. Verheijen, Jeroen C.; Van der Marel, Gijsbert A.; Van Boom, Jacques H.; Bayly, Suzanne F.; Player, Mark R.; Torrence, Paul F. (Gorlaeus Laboratories, Leiden Institute of Chemistry, Leiden, 2300 RA, Neth.). Bioorganic & Medicinal Chemistry, 7(3), 449-455 (English) 1999. CODEN: BMECEP. ISSN: 0968-0896. Publisher: Elsevier Science Ltd..

AB To potentiate the 2-5A (2',5'-oligoadenylate)-antisense and peptide nucleic acid (PNA) approaches to regulation of gene expression, composite mols. were generated contg. both 2-5A and PNA moieties. 2-5A-PNA adducts were synthesized using solid-phase techniques. Highly cross-linked polystyrene beads were functionalized with glycine tethered through a p-hydroxymethyl-benzoic acid linker and the PNA domain of the chimeric oligonucleotide analog was added by sequential elongation of the amino terminus with the monomethoxytrityl protected N-(2-aminoethyl)-N-(adenin-1-ylacetyl)glycinate. Transition to the 2-5A domain was accomplished by coupling of the PNA chain to dimethoxytrityl protected N-(2-hydroxyethyl)-N-(adenin-1-ylacetyl)glycinate. Finally, (2-cyanoethyl)-N,N-diisopropyl-4-O-(4,4-dimethoxytrityl)butylphosphoramidite and the corresponding (2-cyanoethyl)-N,N-diisopropylphosphoramidite of 5-O-(4,4'-dimethoxytrityl)-3-O-(tert-butyl-dimethylsilyl)-N6-benzoyl-adenosine were the synthons employed to add the 2 butanediol phosphate linkers and the four 2',5'-linked riboadenylates. The 5'-phosphate moiety was introduced with 2-[[2-(4,4'-dimethoxytrityloxy)ethyl]sulfonyl]ethyl-(2-cyanoethyl)-N,N-diisopropylphosphoramidite. Deprotection with methanolic NH₃ and tetraethylammonium fluoride afforded the desired products, 2-5A-pnaA4, 2-5A-pnaA8 and 2-5A-pnaA12. When evaluated for their ability to cause the degrading of two different RNA substrates by the 2-5A-dependent RNase L, these new 2-5A-PNA conjugates were found to be potent RNase L activators. The union of 2-5A and PNA presents fresh opportunities to explore the biol. and therapeutic implications of these unique approaches to antisense.

L13 ANSWER 21 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 224782-67-6 REGISTRY
 CN Triphosphoric acid, P-[4-(6-amino-9H-purin-9-yl)-2-(hydroxymethyl)-2-butenyl] ester (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C10 H16 N5 O11 P3
 SR CA
 LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

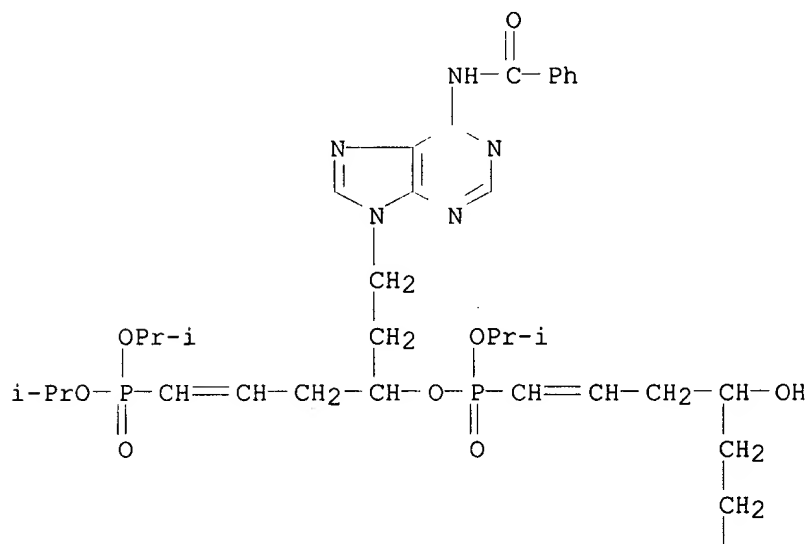
REFERENCE 1: 130:352181 An allylic/acyclic adenosine nucleoside triphosphate for termination of DNA synthesis by DNA template-dependent polymerases. Martinez, Carlos I.; Thoresen, Lars H.; Gibbs, Richard A.; Burgess, Kevin (Department of Chemistry, Texas A and M University, College Station, TX, 77842-3012, USA). Nucleic Acids Research, 27(5), 1271-1274 (English) 1999. CODEN: NARHAD. ISSN: 0305-1048. Publisher: Oxford University Press.

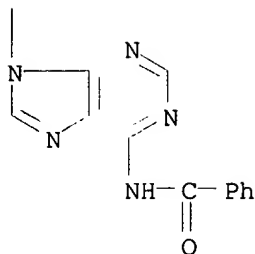
AB An allylic ATP analog (AATP) was tested as a substrate for com. available

DNA polymerases. All but one of the enzymes assayed incorporated AATP opposite thymidine (T) with concomitant termination of the elongation reaction. A concn. of only 1 .mu.M was sufficient for complete termination of the polymn. reaction for a short template mediated by Ampli Taq DNA polymerase FS (Taq FS). This result suggests that AATP could be used as a 2',3'-dideoxyadenosine-5'-triphosphate (ddA) surrogate. Kinetics of incorporation revealed that AATP was 48 times less efficiently incorporated than ddA. Furthermore, AATP was used in dye-primer sequencing as a substitute for ddA.

L13 ANSWER 22 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 223409-57-2 REGISTRY
 CN Phosphonic acid, [6-[6-(benzoylamino)-9H-purin-9-yl]-4-[[[6-[6-(benzoylamino)-9H-purin-9-yl]-4-hydroxy-1-hexenyl](1-methylethoxy)phosphinyl]oxy]-1-hexenyl]-, bis(1-methylethyl) ester (9CI)
 (CA INDEX NAME)
 FS 3D CONCORD
 MF C45 H56 N10 O9 P2
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:296947 Synthesis of acyclic carba-nucleoside phosphonates, structural analogs to natural deoxyribonucleotides. Esposito, Annamaria; Perino, Maria Grazia; Taddei, Maurizio (Dipartimento Chimica, Universita Sassari, Sassari, I-07100, Italy). European Journal of Organic Chemistry (4), 931-936 (English) 1999. CODEN: EJOCFK. ISSN: 1434-193X. Publisher: Wiley-VCH Verlag GmbH.

AB Acyclic carba-nucleoside phosphonates, modeled on natural deoxyribonucleotides were prepd. starting from DNA nucleobases and tert-Bu acrylate. The products obtained from a Michael-type reaction were elongated to .beta.-oxo esters that were first reduced to .beta.-hydroxy esters and then transformed into protected .beta.-hydroxy aldehydes. Wittig-Horner-Emmons reaction with the anion of CH₂[PO(OCHMe₂)₂]₂ gave, after deprotection, the desired 4-hydroxy-6-purinyl- or -6-pyrimidinyl-1-hexenylphosphonates. A dimer, potential precursor of acyclic polynucleotides (APN), homomorphous with DNA, was also prepd.

L13 ANSWER 23 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 206646-04-0 REGISTRY

CN Phosphoric acid, monoanhydride with [[(1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy)methyl]phosphonic acid (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)-1-methylethoxy)methyl]phosphonic acid, (R)-

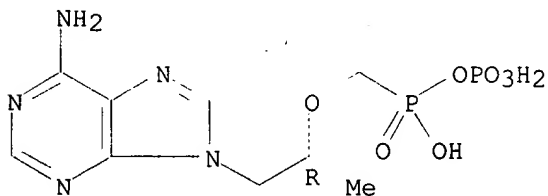
FS STEREOSEARCH

MF C9 H15 N5 O7 P2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

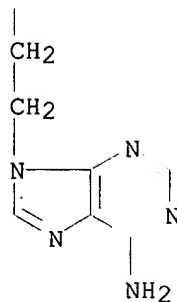
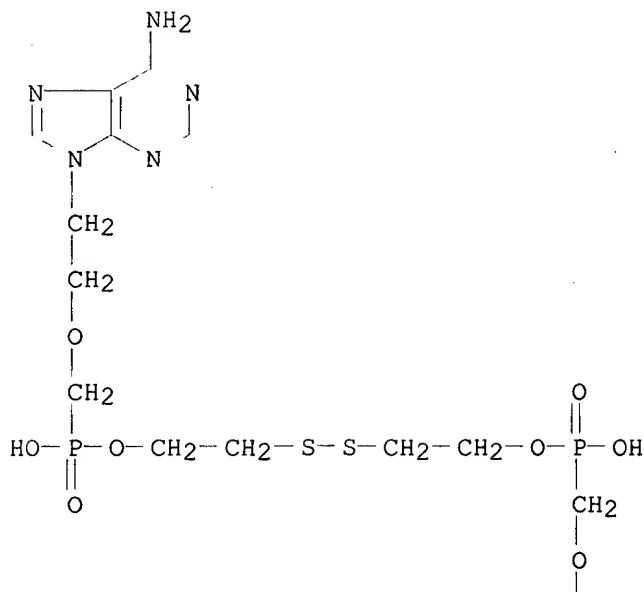
- REFERENCE 1: 136:148 Metabolism of GS-7340, a novel phenyl monophosphoramidate intracellular prodrug of PMPA, in blood. Eisenberg, Eugene J.; He, Gong-Xin; Lee, William A. (Gilead Sciences, Foster City, CA, USA). Nucleosides, Nucleotides & Nucleic Acids, 20(4-7), 1091-1098 (English) 2001. CODEN: NNNAFY. ISSN: 1525-7770. Publisher: Marcel Dekker, Inc..
- AB PMPA, an acyclic nucleoside phosphonate analog, is a potent inhibitor of HIV. In the cells, PMPA is efficiently phosphorylated by intracellular kinases to produce PMPApp, the pharmacol. active metabolite. Despite its demonstrated antiviral potency, PMPA has limited cell permeability presumably resulting from the presence of two neg. charges on the phosphonyl group. To enhance intracellular concns. of PMPA, we developed a prodrug, selectively metabolized inside cells. GS-7340 (9-[(R)-2-[[[(S)-1-(isopropoxycarbonyl)ethyl]amino]phenoxy-phosphinyl]methoxy] propyl]adenine) is a prodrug which is orally bioavailable in dogs as the intact prodrug and has demonstrated anti-HIV activity in cell culture of over 1000-fold greater than that of PMPA. The metab. of PMPA in peripheral blood mononuclear cells (PBMC), red blood cells (RBC) and plasma was examd. following exposure of whole blood to PMPA or GS-7340 at concns. similar to ones obsd. systemically following oral administration in dogs. Following 1 h incubation with whole blood, GS-7340 was stable in plasma, produced high levels of PMPA and its phosphorylated metabolites in PBMC but not in RBC. No intact prodrug was present in PBMC. The only other species present in PBMC was monoalaninyl PMPA. The levels of PMPA and the phosphorylated metabolites were over 20 times greater than those after incubation with PMPA. The dog and human blood data were similar. The intracellular levels of PMPA and PMPApp were roughly proportional to GS-7340 over a 10-fold concn. range indicating a lack of saturability of uptake and phosphorylation. Since PMPApp is the species responsible for antiviral activity of PMPA, the high intracellular levels of PMPApp should be an important indicator of greater clin. efficacy of GS-7340.
- REFERENCE 2: 131:237529 Effect of acyclic nucleoside phosphonates on the HIV-1 integrase in vitro. Abu, Sheika G.; Tramontano, E.; Loi, A. G.; Franchetti, P.; Grifantini, M.; La Colla, P. (Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, 62032, Italy). Nucleosides & Nucleotides, 18(4 & 5), 849-851 (English) 1999. CODEN: NUNUD5. ISSN: 0732-8311. Publisher: Marcel Dekker, Inc..
- AB Integrase (IN) is an essential enzyme in the human immunodeficiency virus type-1 (HIV-1) replication cycle and, thus, a potential target for chemotherapeutic agents. Because various nucleotide analogs have been reported to inhibit IN in vitro, we investigated the effect of acyclic nucleoside phosphonates. Both unphosphorylated and diphosphorylated derivs. were inhibitory to IN at concns. ranging between 60 and 800 .mu.M, with diphosphorylated derivs. being 5- to 8-fold more potent than unphosphorylated counterparts.
- REFERENCE 3: 130:60635 Selective inhibition of HIV-1 reverse transcriptase by an antiviral inhibitor, (R)-9-(2-phosphonylmethoxypropyl)adenine. Suo, Zucal; Johnson, Kenneth A. (Department of Biochemistry and Molecular Biology, the Pennsylvania State University, University Park, PA, 16802, USA). Journal of Biological Chemistry, 273(42), 27250-27258 (English) 1998. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.
- AB (R)-9-(2-Phosphonylmethoxypropyl)adenine (PMPA) is an acyclic nucleoside phosphonate that has been shown to be effective in the treatment of AIDS although it has a shorter sepn. between the adenine and phosphorus than dideoxy-AMP and dAMP. By using presteady state kinetic methods, we examd. the incorporation of the diphosphate of PMPA, 2',3'-dideoxyadenosine

5'-triphosphate (ddATP), and dATP catalyzed by wild-type human immunodeficiency virus type 1 (HIV-1) reverse transcriptase, an exonuclease-deficient T7 DNA polymerase (T7 exo-), and wild-type rat DNA polymerase .beta. to evaluate the selectivity of PMPA as an antiviral inhibitor. With a DNA/DNA or DNA/RNA 22/43-mer duplex, the diphosphate of PMPA (PMPApp) is as effective as ddATP in reactions catalyzed by HIV-1 reverse transcriptase in that both analogs have similar substrate specificity consts. (kp/Kd) which are only 5-fold lower than dATP. In contrast, PMPApp is a much weaker inhibitor of the reaction catalyzed by T7 exo- (with the DNA/DNA 22/43-mer duplex) in that PMPApp has a 5.times.10-4-fold lower kp/Kd than ddATP and dATP. The lower kp/Kd of PMPApp is due to a 1000-2000-fold lower incorporation rate (kp) and a 35-45-fold lower binding const. (Kd). Similarly, PMPApp is 800-fold less inhibitory toward polymerase .beta. with the DNA/DNA 22/43-mer duplex, whereas in studies with a single nucleotide gapped DNA (22-20/43-mer) PMPApp is 13-fold less inhibitory than ddATP. Although parallel studies will need to be performed using appropriate human polymerases, these results begin to define the mechanistic basis for the reported lower toxicity of PMPA in the treatment of AIDS.

REFERENCE 4: 128:303669 Anti-human immunodeficiency virus activity and cellular metabolism of a potential prodrug of the acyclic nucleoside phosphonate 9-R-(2-phosphonomethoxypropyl)adenine (PMPA), bis(isopropylloxymethylcarbonyl)PMPA. Robbins, Brian L.; Srinivas, Ranga V.; Kim, Choung; Bischofberger, Norbert; Fridland, Arnold (Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA). Antimicrobial Agents and Chemotherapy, 42(3), 612-617 (English) 1998. CODEN: AMACQ. ISSN: 0066-4804. Publisher: American Society for Microbiology.

AB Bis(isopropylloxymethylcarbonyl) 9-R-(2-phosphonomethoxypropyl)adenine [bis(POC)PMPA] has been identified as a novel prodrug of PMPA. The anti-human immunodeficiency virus activity of bis(POC)PMPA was >100-fold greater than that of PMPA in both an established T-cell line and primary peripheral blood lymphocytes. This improved efficacy was shown to be due to a rapid intracellular uptake of the prodrug resulting in an increased intracellular accumulation of PMPA diphosphate (PMPApp), the pharmacol. active metabolite. PMPApp levels in bis(POC)PMPA-treated cells exceeded by >1000-fold the levels seen in cells treated with unmodified PMPA in both resting and activated peripheral blood lymphocytes. Significant differences in the intracellular catabolism of PMPA metabolites were noted between the resting and activated lymphocytes. The half-life for the disappearance of PMPApp, derived from either bis(POC)PMPA or PMPA, was 12 to 15 h in the activated lymphocytes and 33 to 50 h in the resting lymphocytes. This long persistence of PMPApp, particularly in resting lymphocytes, may be unique to the nucleoside phosphonate analogs and indicates that effective levels of the active metabolite can be achieved and maintained with relatively infrequent administration of the parent drug.

L13 ANSWER 24 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 205813-51-0 REGISTRY
 CN Phosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy]methyl]-, dithiodi-2,1-ethanediyl ester (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C20 H30 N10 O8 P2 S2
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

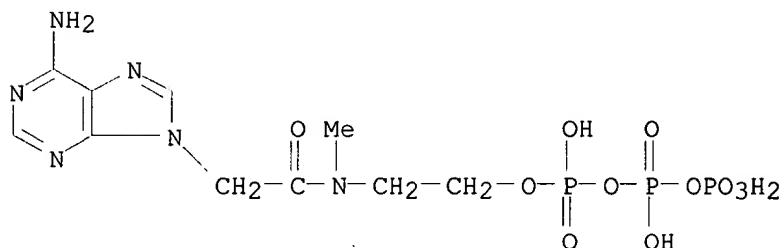
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:278609 Comparison of the disposition of ester prodrugs of the antiviral agent 9-(2-phosphonylmethoxyethyl)adenine [PMEA] in Caco-2 monolayers. Annaert, P.; Gosselin, G.; Pompon, A.; Benzaria, S.; Valette, G.; Imbach, J. - L.; Naesens, L.; Hatse, S.; De Clercq, E.; Van Den Mooter, G.; Kinget, R.; Augustijns, P. (Laboratorium voor Farmacotechnologie en Biofarmacie, KULeuven, Louvain, B-3000, Belg.). Pharmaceutical Research, 15(2), 239-245 (English) 1998. CODEN: PHREEB. ISSN: 0724-8741. Publisher: Plenum Publishing Corp..

AB To evaluate the potential of several bis-ester prodrugs of the antiviral agent 9-(2-phosphonylmethoxyethyl)adenine (PMEA, adefovir) to enhance the oral absorption of PMEA. Caco-2 monolayers were used to est. intestinal

transport and metab. of the bis(pivaloyloxymethyl)-ester [bis(POM)-] and a series of bis(S-acyl-2-thioethyl)-esters [bis(SATE)-] of PMEAs. An LC-MS method was used for the identification of unknown metabolites which were formed from the SATE-esters. During transport across Caco-2 monolayers, all esters were extensively degraded as could be concluded from the appearance of the mono-ester and free PMEAs in apical as well as basolateral compartments. Incubation of SATE-esters with the monolayers resulted in the formation of two addnl. metabolites, which were identified as 2-thioethyl-PMEA and its dimerization product. All ester prodrugs resulted in enhanced transepithelial transport of total PMEAs (i.e. the bis-esters and their corresponding metabolites, including PMEAs), but significant differences could be obsd. between the various esters. Transport of total PMEAs ranged from 0.4 \pm 0.1% for the bis[S(methyl)ATE]-ester to 15.3 \pm 0.9% for the more lipophilic bis[S(phenyl)ATE]-PMEA. A relationship between total transport of the esters and their lipophilicity (as estd. by their octanol/water partition coeff.) was established ($r^2 = 0.87$). Incubation of prodrug esters with homogenates from Caco-2 cells showed large differences in susceptibility of the compds. to esterases, the half-lives of the bis-esters varying from 4.3 \pm 0.3 min for the bis[S(phenyl)ATE]-PMEA to 41.5 \pm 0.8 min for its Me analog. In addn., intracellularly formed PMEAs were obsd. to be further converted by the cells to the diphosphorylated PMEAs (PMEApp). Several SATE-esters of PMEAs can be considered as potential alternatives to bis(POM)-PMEAs, due to enhanced epithelial transport, sufficient chem. and enzymic stability and adequate release of PMEAs. Toxicol. studies as well as in vivo expts. are required in order to further explore the potential of those SATE-esters as prodrugs for oral delivery of PMEAs.

L13 ANSWER 25 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 202915-77-3 REGISTRY
 CN Triphosphoric acid, P-[2-[[[(6-amino-9H-purin-9-yl)acetyl]methylamino]ethyl] ester (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C10 H17 N6 O11 P3
 SR CA
 LC STN Files: CA, CAPLUS, CASREACT



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1 REFERENCES IN FILE CA (1967 TO DATE)
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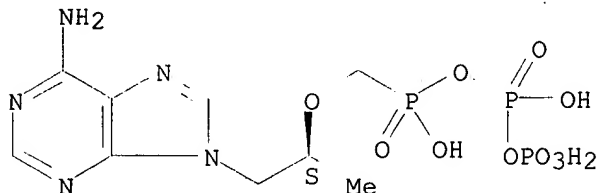
REFERENCE 1: 128:163291 Acyclic nucleoside triphosphate analogs as terminators in biocatalytic DNA replication. Martinez, Carlos I.; Ansari, M. Ali; Gibbs, Richard; Burgess, Kevin (Department of Chemistry, Texas A and M University, College Station, TX, 77843-3255, USA). Bioorganic & Medicinal Chemistry Letters, 7(23), 3013-3016 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..
 AB Acyclic nucleoside triphosphates were prepd. and tested as substrates for

Searched by: Mary Hale 308-4258 CM-1 12D16

several DNA replicating enzymes; AmpliTaq FS and Taquenase accepted these compds. as substrates leading to chain termination.

L13 ANSWER 26 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 182415-40-3 REGISTRY
CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)-1-methylethoxy]methyl]phosphonic acid, (S)- (9CI) (CA INDEX NAME)
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SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

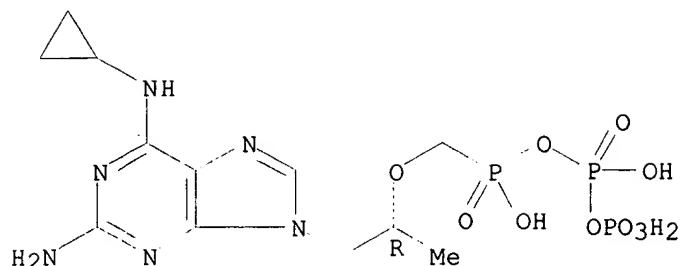
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:268990 Structural features of acyclic nucleotide analogs conferring inhibitory effects on cellular replicative DNA polymerases. Kramata, Pavel; Birkus, Gabriel; Otmar, Miroslav; Votruba, Ivan; Holy, Antonin (Institute Organic Chemistry Biochemistry, Academy Sciences Czech Republic, Prague, 166 10, Czech Rep.). Collect. Czech. Chem. Commun., 61(Spec. Issue), S188-S191 (English) 1996. CODEN: CCCCAK. ISSN: 0010-0765.

AB Diphosphates of phosphonomethoxyalkyl acyclic nucleotide analogs were tested as inhibitors of two proteolyzed forms of cellular repetitive DNA polymerase .epsilon., and DNA polymerases .alpha. and .delta.. The Ki/Km ratios are given. Effects of different substitutions on their inhibitory activity are discussed.

L13 ANSWER 27 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 182411-03-6 REGISTRY
CN Diphosphoric acid, monoanhydride with [[2-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-1-methylethoxy]methyl]phosphonic acid, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C12 H21 N6 O10 P3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:268990 Structural features of acyclic nucleotide analogs conferring inhibitory effects on cellular replicative DNA polymerases. Kramata, Pavel; Birkus, Gabriel; Otmar, Miroslav; Votruba, Ivan; Holy, Antonin (Institute Organic Chemistry Biochemistry, Academy Sciences Czech Republic, Prague, 166 10, Czech Rep.). Collect. Czech. Chem. Commun., 61(Spec. Issue), S188-S191 (English) 1996. CODEN: CCCCAK. ISSN: 0010-0765.

AB Diphosphates of phosphonomethoxyalkyl acyclic nucleotide analogs were tested as inhibitors of two proteolyzed forms of cellular repetitive DNA polymerase .epsilon., and DNA polymerases .alpha. and .delta.. The Ki/Km ratios are given. Effects of different substitutions on their inhibitory activity are discussed.

L13 ANSWER 28 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 182411-02-5 REGISTRY

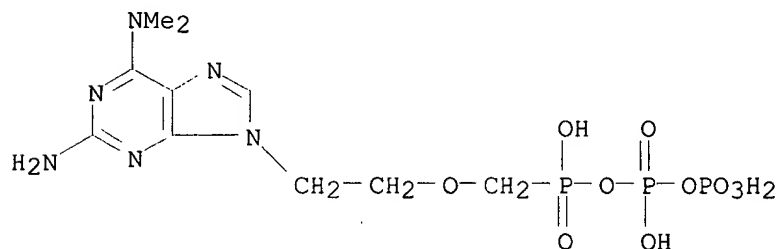
CN Diphosphoric acid, monoanhydride with [[2-[2-amino-6-(dimethylamino)-9H-purin-9-yl]ethoxy)methyl]phosphonic acid (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C10 H19 N6 O10 P3

SR CA

LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:268990 Structural features of acyclic nucleotide analogs conferring inhibitory effects on cellular replicative DNA polymerases. Kramata, Pavel; Birkus, Gabriel; Otmar, Miroslav; Votruba, Ivan; Holy,

Searched by: Mary Hale 308-4258 CM-1 12D16

Antonin (Institute Organic Chemistry Biochemistry, Academy Sciences Czech Republic, Prague, 166 10, Czech Rep.). Collect. Czech. Chem. Commun., 61(Spec. Issue), S188-S191 (English) 1996. CODEN: CCCCAK. ISSN: 0010-0765.

AB Diphosphates of phosphonomethoxyalkyl acyclic nucleotide analogs were tested as inhibitors of two proteolyzed forms of cellular repetitive DNA polymerase .epsilon., and DNA polymerases .alpha. and .delta.. The K_i/K_m ratios are given. Effects of different substitutions on their inhibitory activity are discussed.

L13 ANSWER 29 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-23-1 REGISTRY

CN Phosphoric acid, mono[3-[[[2,3-dihydroxy-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propoxy]hydroxyphosphinyl]oxy]-2-hydroxy-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl] mono[2,3-dihydroxy-1-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl] ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

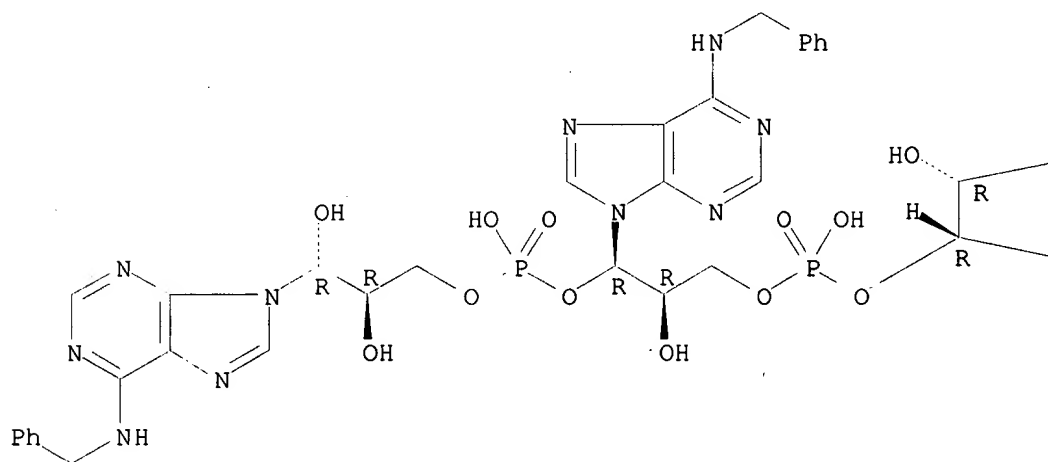
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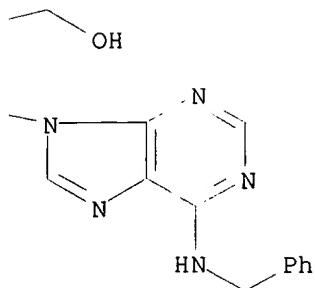
SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.

PAGE 1-A





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1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were proved by UV, CD, and ¹H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)2A.

L13 ANSWER 30 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-21-9 REGISTRY

CN Phosphoric acid, 2-(benzoyloxy)-3-[[[2,3-bis(benzoyloxy)-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propoxy][2-(4-nitrophenyl)ethoxy]phosphinyl]oxy]-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl 2-(benzoyloxy)-3-hydroxy-1-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl 2-(4-nitrophenyl)ethyl ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

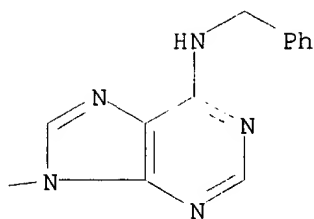
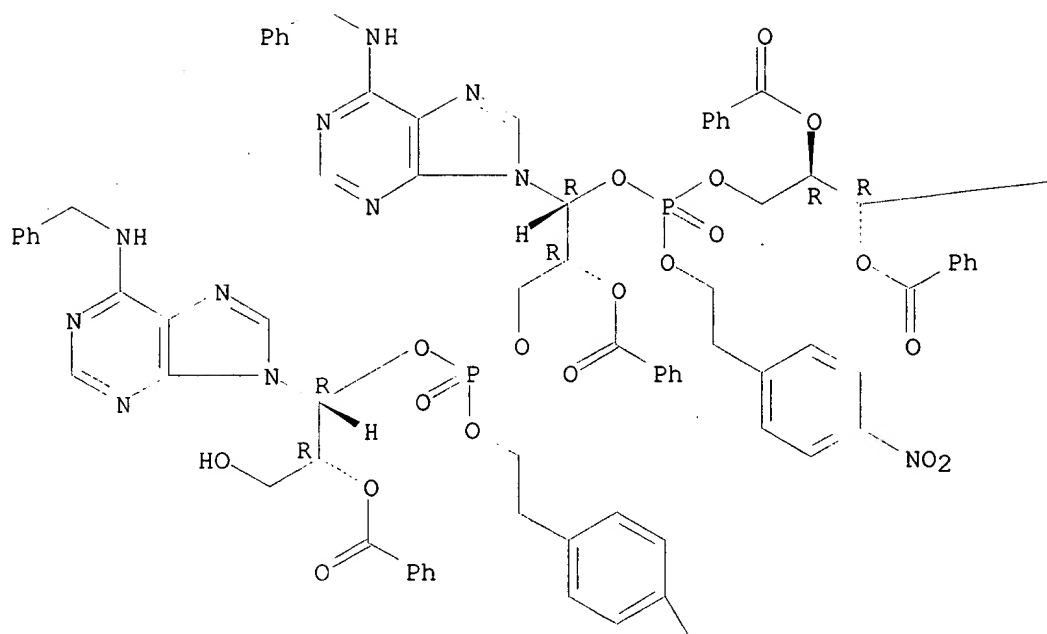
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MF C89 H79 N17 O21 P2

SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.

NO₂

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were

proved by UV, CD, and ¹H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)₂A.

L13 ANSWER 31 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-19-5 REGISTRY

CN Phosphoric acid, 2-(benzoyloxy)-3-[[[2,3-bis(benzoyloxy)-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propoxy][2-(4-nitrophenyl)ethoxy]phosphinyl]oxy]-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl 2-(benzoyloxy)-3-[(4-methoxyphenyl)diphenylmethoxy]-1-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl 2-(4-nitrophenyl)ethyl ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

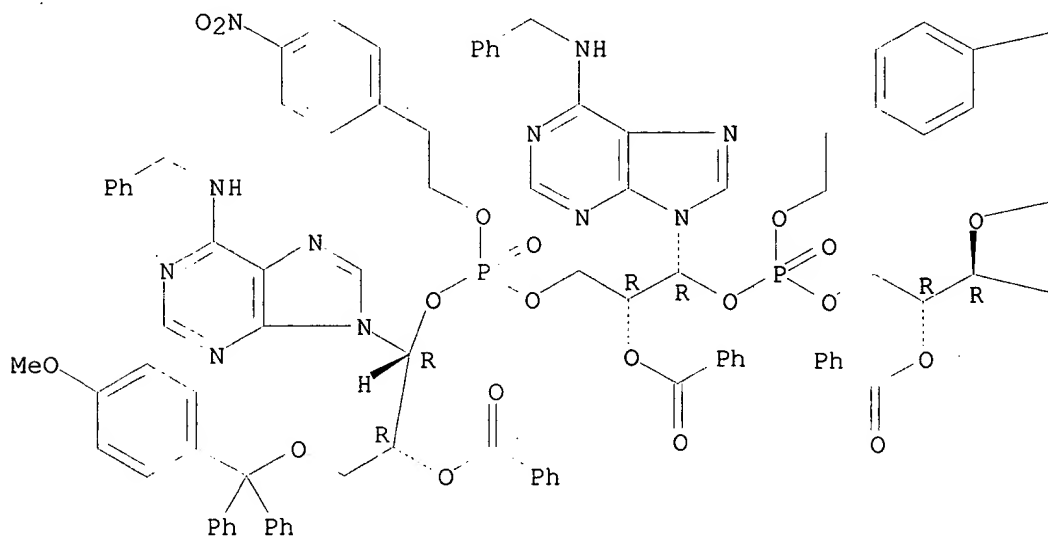
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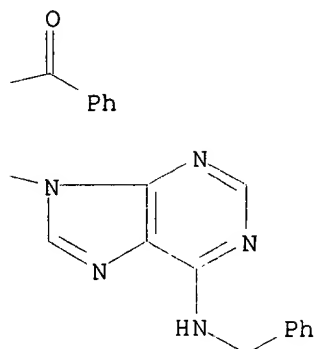
SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.

PAGE 1-A



—NO₂

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1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were proved by UV, CD, and ¹H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)2A.

L13 ANSWER 32 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-17-3 REGISTRY

CN Phosphoric acid, mono[3-(6-amino-9H-purin-9-yl)-3-[[[3-(6-amino-9H-purin-9-yl)-2,3-dihydroxypropoxy]hydroxyphosphinyl]oxy]-2-hydroxypropyl] mono[2,3-dihydroxy-1-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl] ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

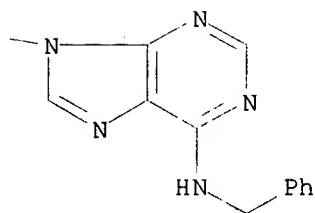
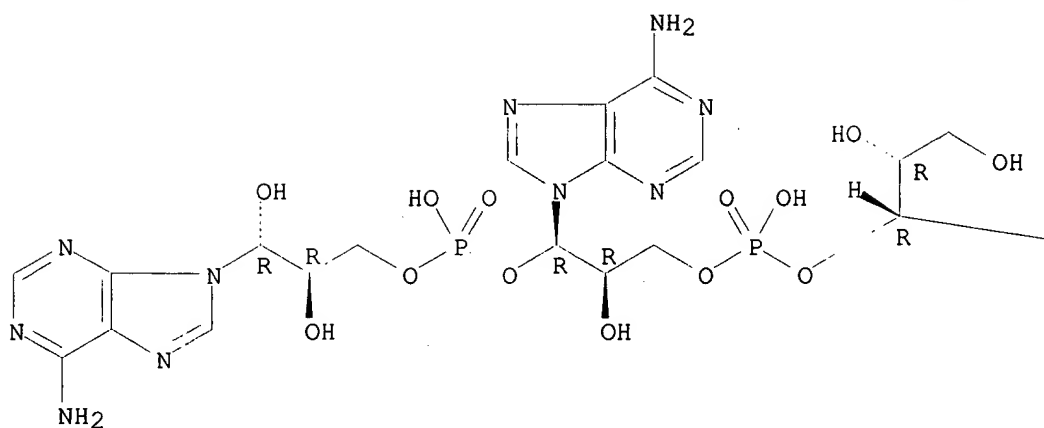
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MF C31 H37 N15 O13 P2

SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were proved by UV, CD, and 1H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)2A.

L13 ANSWER 33 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-15-1 REGISTRY

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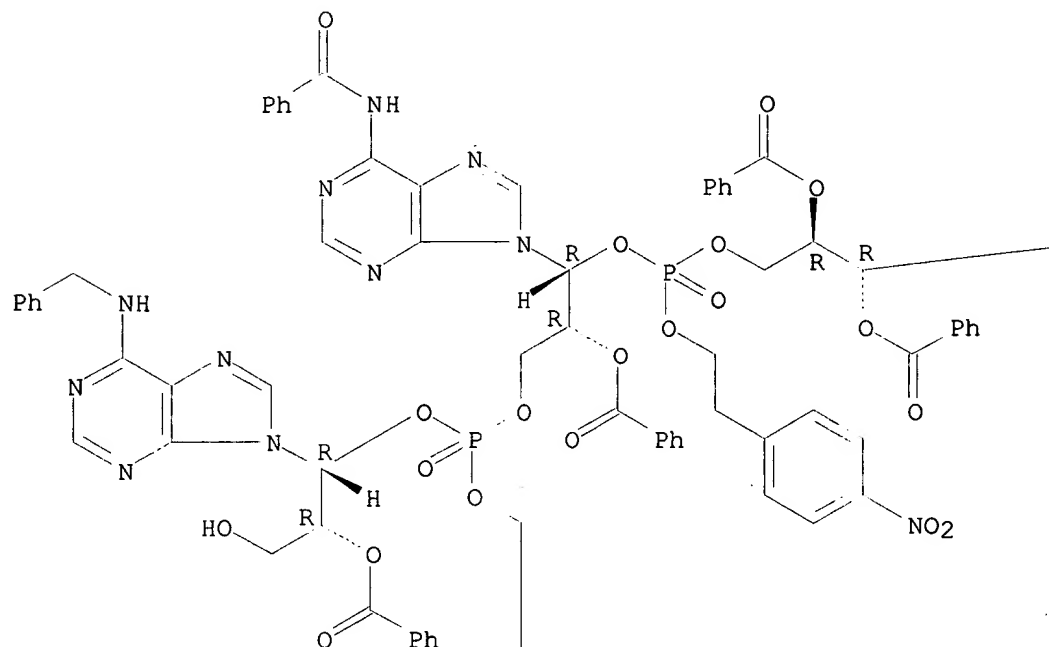
Searched by: Mary Hale 308-4258 CM-1 12D16

(benzoylamino)-9H-purin-9-yl]-2,3-bis(benzoyloxy)propoxy][2-(4-nitrophenyl)ethoxy]phosphinyl]oxy]-2-(benzoyloxy)propyl
 2-(benzoyloxy)-3-hydroxy-1-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl
 2-(4-nitrophenyl)ethyl ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA
 INDEX NAME)

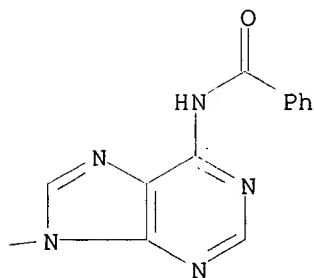
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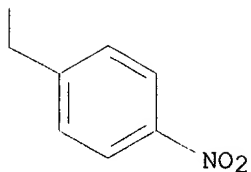
Relative stereochemistry.

PAGE 1-A



PAGE 1-B





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were proved by UV, CD, and 1H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)2A.

L13 ANSWER 34 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-13-9 REGISTRY

CN Phosphoric acid, 3-[6-(benzoylamino)-9H-purin-9-yl]-3-[[[3-[6-(benzoylamino)-9H-purin-9-yl]-2,3-bis(benzoyloxy)propoxy][2-(4-nitrophenyl)ethoxy]phosphinyl]oxy]-2-(benzoyloxy)propyl 2-(benzoyloxy)-3-[(4-methoxyphenyl)diphenylmethoxy]-1-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl 2-(4-nitrophenyl)ethyl ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

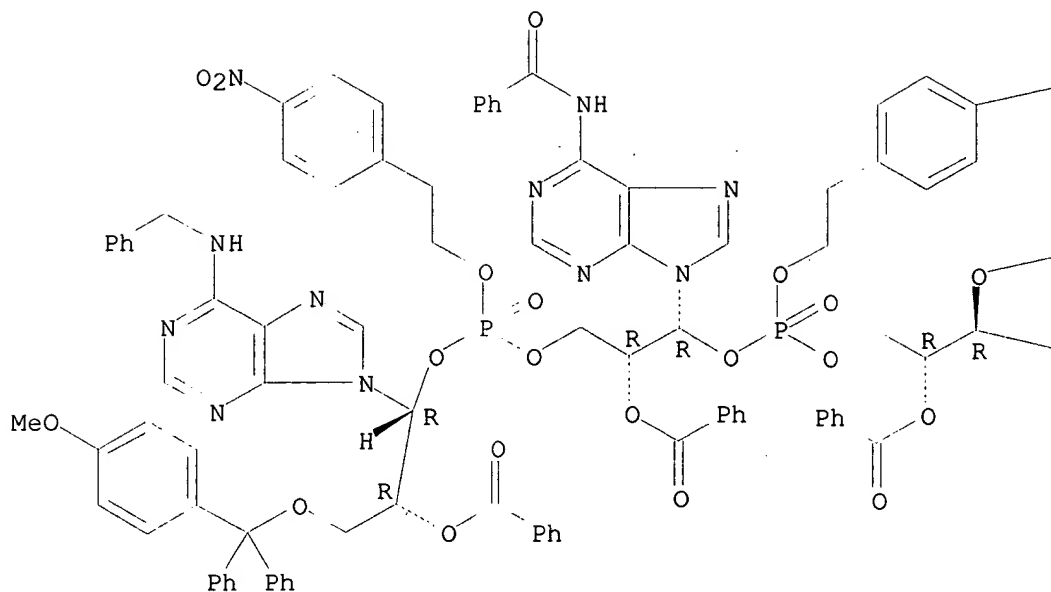
FS STEREOSEARCH

MF C109 H91 N17 O24 P2

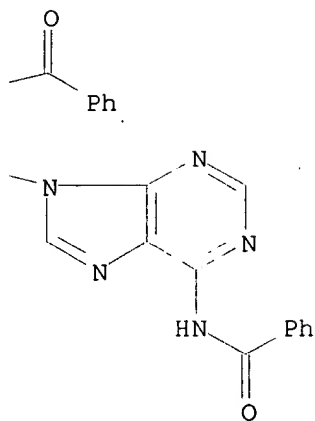
SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.



—NO₂



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem.,

Searched by: Mary Hale 308-4258 CM-1 12D16

Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were proved by UV, CD, and ¹H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)2A.

L13 ANSWER 35 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-12-8 REGISTRY

CN Phosphoric acid, mono[3-[[[3-(6-amino-9H-purin-9-yl)-2,3-dihydroxypropoxy]hydroxyphosphinyl]oxy]-2-hydroxy-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl] mono[1-(6-amino-9H-purin-9-yl)-2,3-dihydroxypropyl] ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

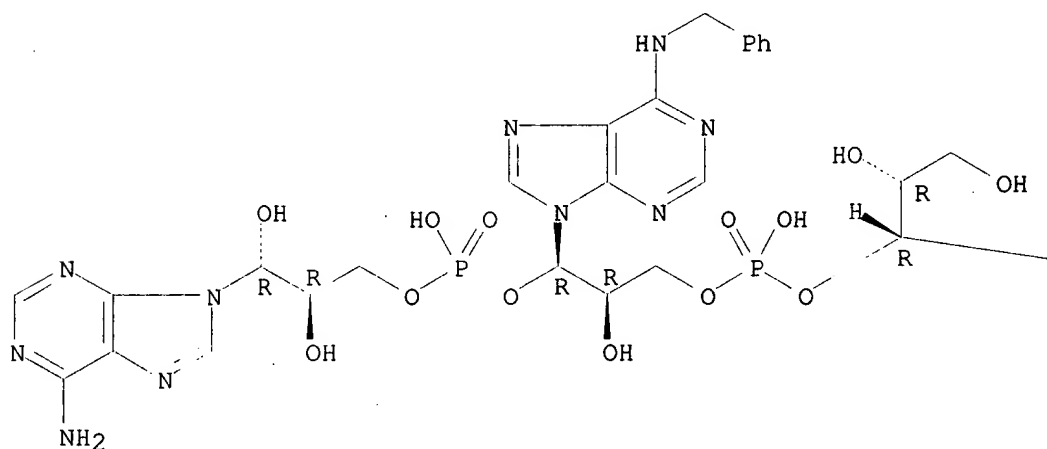
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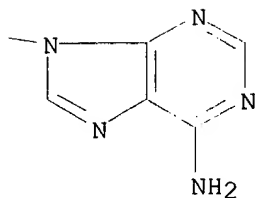
SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were proved by UV, CD, and 1H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)2A.

L13 ANSWER 36 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-10-6 REGISTRY

CN Phosphoric acid, 1-[6-(benzoylamino)-9H-purin-9-yl]-2-(benzoyloxy)-3-hydroxypropyl 3-[[[3-[6-(benzoylamino)-9H-purin-9-yl]-2,3-bis(benzoyloxy)propoxy][2-(4-nitrophenyl)ethoxy]phosphinyl]oxy]-2-(benzoyloxy)-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl 2-(4-nitrophenyl)ethyl ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

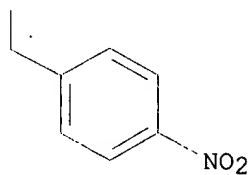
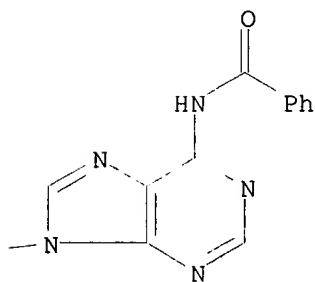
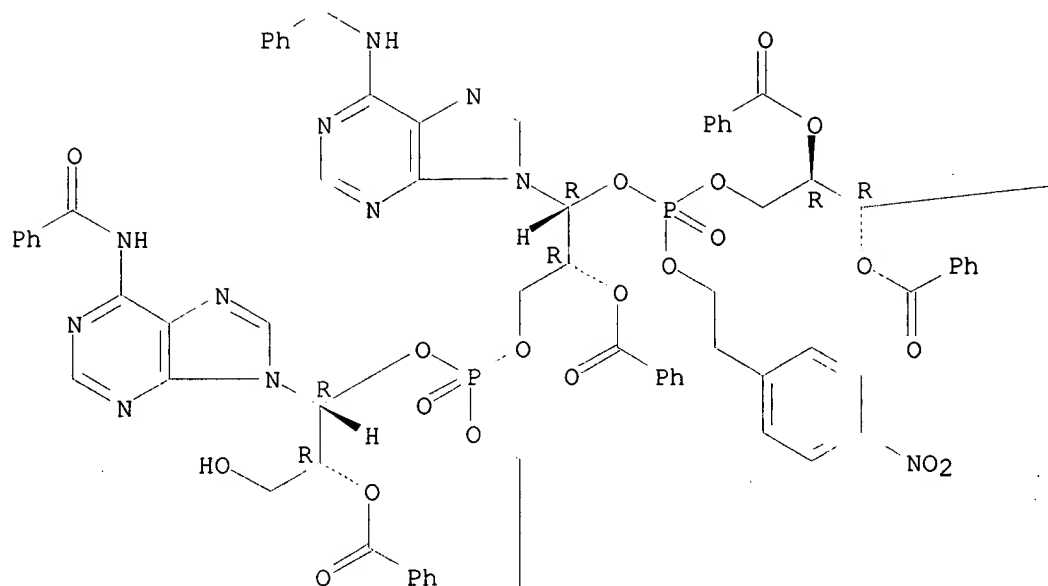
FS STEREOSEARCH

MF C89 H75 N17 O23 P2

SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.;

Searched by: Mary Hale 308-4258 CM-1 12D16

Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were proved by UV, CD, and ¹H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)2A.

L13 ANSWER 37 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-08-2 REGISTRY

CN Phosphoric acid, 1-[6-(benzoylamino)-9H-purin-9-yl-2-(benzoyloxy)-3-[(4-methoxyphenyl)diphenylmethoxy]]propyl 3-[[[3-[6-(benzoylamino)-9H-purin-9-yl]-2,3-bis(benzoyloxy)propoxy][2-(4-nitrophenyl)ethoxy]phosphinyl]oxy]-2-(benzoyloxy)-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propyl 2-(4-nitrophenyl)ethyl ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

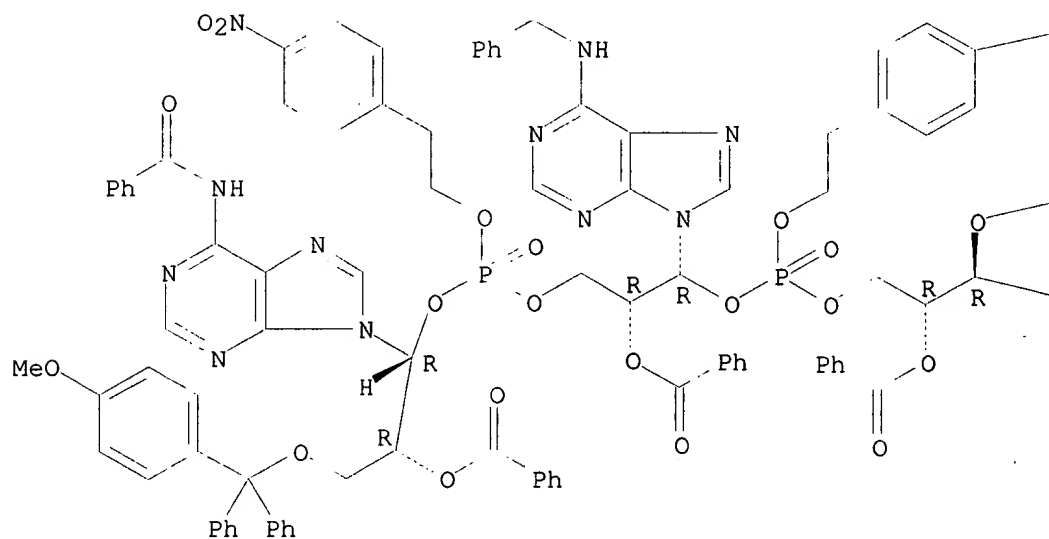
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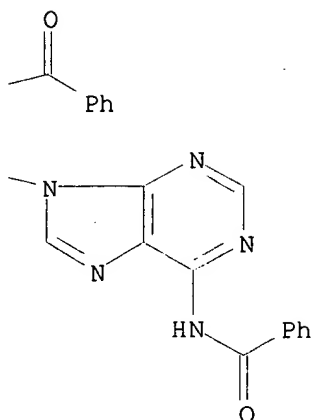
SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.

PAGE 1-A



—NO₂

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were proved by UV, CD, and ¹H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)2A.

L13 ANSWER 38 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-06-0 REGISTRY

CN Phosphoric acid, mono[3-(6-amino-9H-purin-9-yl)-3-[[[2,3-dihydroxy-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propoxy]hydroxyphosphinyl]oxy]-2-hydroxypropyl] mono[1-(6-amino-9H-purin-9-yl)-2,3-dihydroxypropyl] ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

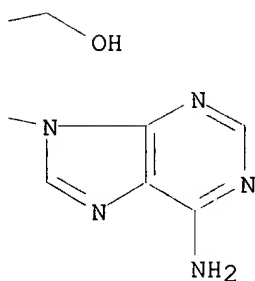
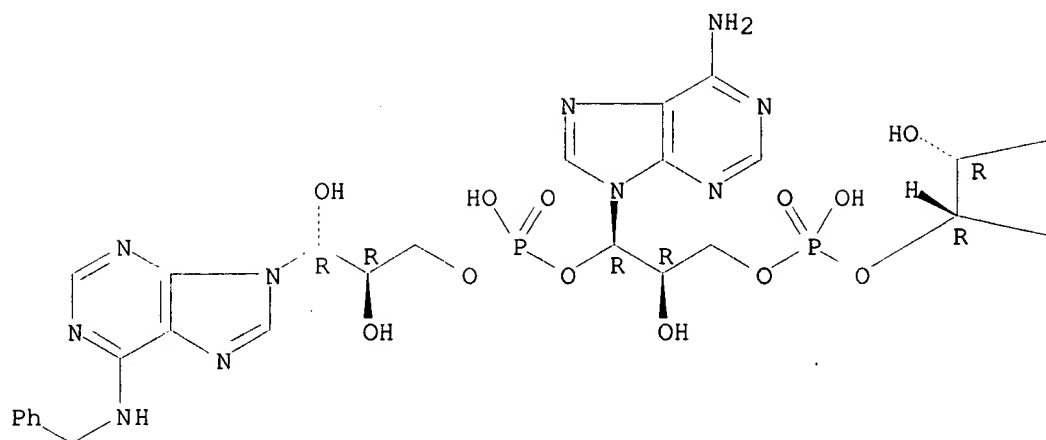
FS STEREOSEARCH

MF C31 H37 N15 O13 P2

SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prep'd. were proved by UV, CD, and ¹H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)2A.

L13 ANSWER 39 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-04-8 REGISTRY

CN Phosphoric acid, 3-[6-(benzoylamino)-9H-purin-9-yl]-2-(benzoyloxy)-3-

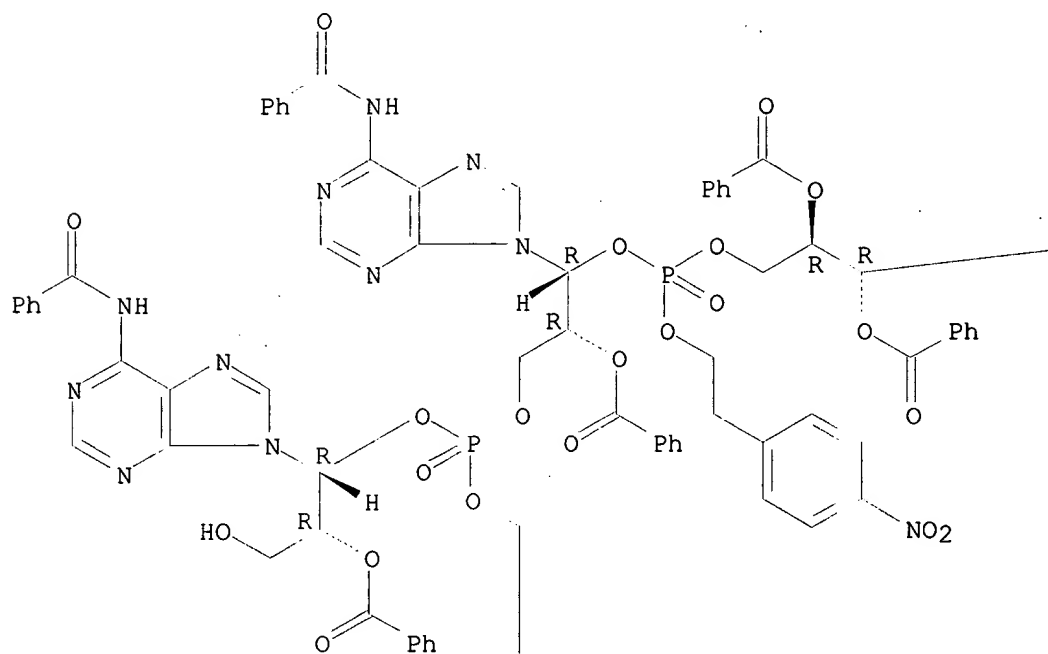
Searched by: Mary Hale 308-4258 CM-1 12D16

[[[2,3-bis(benzoyloxy)-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propoxy][2-(4-nitrophenyl)ethoxy]phosphinyl]oxy]propyl 1-[6-(benzoylamino)-9H-purin-9-yl]-2-(benzoyloxy)-3-hydroxypropyl 2-(4-nitrophenyl)ethyl ester;
 [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

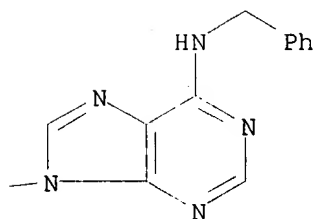
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 LC STN Files: CA, CAPLUS

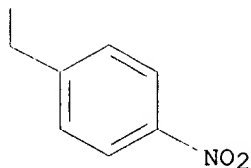
Relative stereochemistry.

PAGE 1-A



PAGE 1-B





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

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L13 ANSWER 40 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 181260-02-6 REGISTRY

CN Phosphoric acid, 3-[6-(benzoylamino)-9H-purin-9-yl]-2-(benzoyloxy)-3-[[[2,3-bis(benzoyloxy)-3-[6-[(phenylmethyl)amino]-9H-purin-9-yl]propoxy][2-(4-nitrophenyl)ethoxy]phosphinyl]oxy]propyl 1-[6-(benzoylamino)-9H-purin-9-yl]-2-(benzoyloxy)-3-[(4-methoxyphenyl)diphenylmethoxy]propyl 2-(4-nitrophenyl)ethyl ester, [1R*[2R*,3R*(2R*,3R*)],2R*]- (9CI) (CA INDEX NAME)

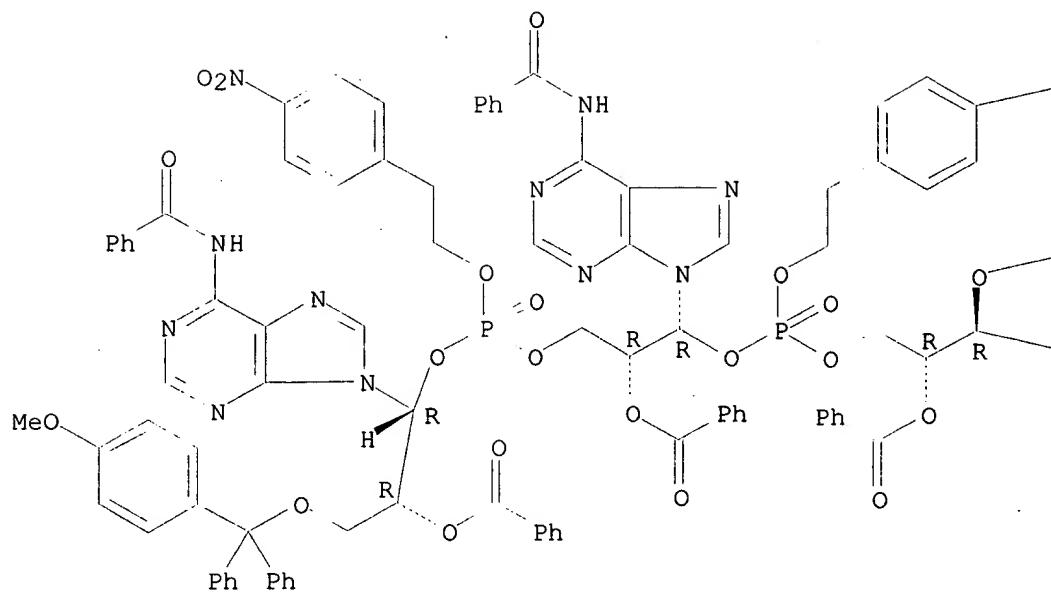
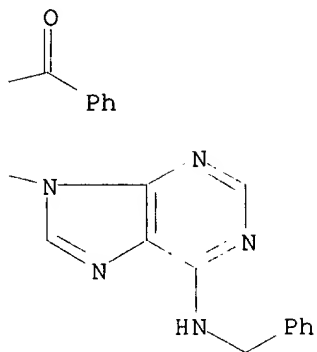
FS STEREOSEARCH

MF C109 H91 N17 O24 P2

SR CA

LC STN Files: CA, CAPLUS

Relative stereochemistry.

—NO₂

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:222336 N6-Benzyladenosine analogs of (A2'p)2A: synthesis and activity toward tobacco mosaic virus. Kvasyuk, E. I.; Kulak, T. I.; Zinchenko, A. I.; Barai, V. N.; Mikhailopulo, I. A. (Inst. Bioorg. Chem., Belaruss. Acad. Sci., Minsk, 220141, Belarus). Bioorg. Khim., 22(3), 208-214 (Russian) 1996. CODEN: BIKHD7. ISSN: 0132-3423.

AB Analogs of (2'-5')oligoadenylate trimer with N6-benzyladenosine in various

positions of the chain and the fully substituted trimer were synthesized by the phosphotriester method. The structures of compds. prepd. were proved by UV, CD, and ¹H NMR. The products inhibit replication of tobacco mosaic virus at 10⁻⁸-10⁻⁶ M, which is comparable to that of natural triadenylate (A2'p)₂A.

L13 ANSWER 41 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 176210-01-8 REGISTRY

CN Phosphoric acid, [2-[[[2-[[[2-(2-amino-1,6-dioxo-9H-purin-9-yl)-2-hydroxyethoxy]methoxyphosphinyl]oxy]-2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methoxyphosphinyl]oxy]-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)]ethyl 2-[[[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]methoxyphosphinyl]oxy]-1-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethyl methyl ester, stereoisomer (9CI) (CA INDEX NAME)

FS STEREOSEARCH

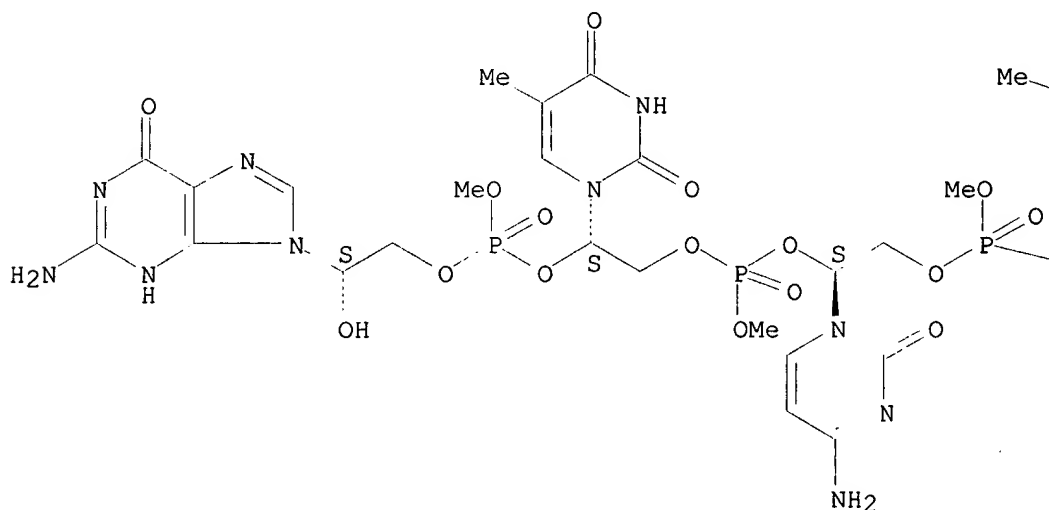
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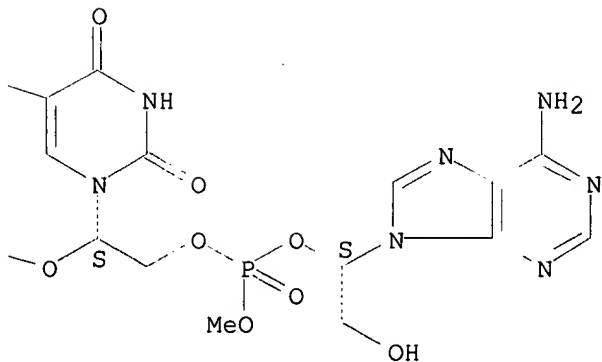
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:115049 N-Pent-4-enoyl nucleoside: application in the synthesis of support-bound and free oligonucleotide analogs by the H-phosphonate approach. Iyer, Radhakrishnan P.; Devlin, Theresa; Habus, Ivan; Ho, Nan-Hui; Yu, Dong; Agrawal, Sudhir (Hybridon Inc., Worcester, MA, 01605, USA). Tetrahedron Lett., 37(10), 1539-42 (English) 1996. CODEN: TELEAY. ISSN: 0040-4039.

AB N-pent-4-enoyl nucleoside H-phosphonates are versatile building blocks for the synthesis of support-bound and free oligonucleotide analogs.

L13 ANSWER 42 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 173298-44-7 REGISTRY

CN Carbamimidic acid, [6-[[3-[[9-(1,3-diformyl-6,8,8-trihydroxy-6,8-dioxido-2,5,7-trioxa-6,8-diphosphaoct-1-yl)-9H-purin-6-yl]amino]-1-oxopropyl]amino]hexyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

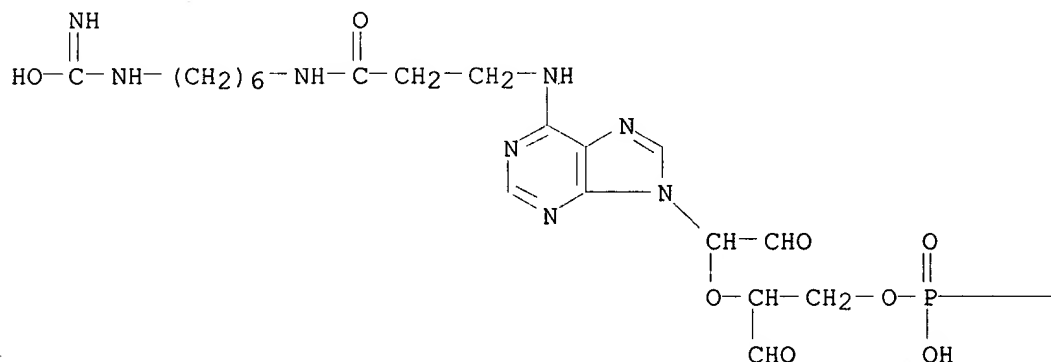
CN Carbamimidic acid, [6-[[3-[[9-(1,3-diformyl-6,8,8-trihydroxy-2,5,7-trioxa-6,8-diphosphaoct-1-yl)-9H-purin-6-yl]amino]-1-oxopropyl]amino]hexyl]-, P,P'-dioxide

MF C20 H32 N8 O12 P2

CI COM

SR CA

PAGE 1-A



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L13 ANSWER 43 OF 166  REGISTRY  COPYRIGHT 2002 ACS
RN 172541-87-6  REGISTRY
CN Tetraphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [R-(R*,R*)]-(9CI)  (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H15 N5 O16 P4
SR CA
LC STN Files:  CA, CAPLUS
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1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

polyphosphates, .epsilon.-(ApnA), are used as artificial fluorogenic substrates. Ap4Aase exhibits a mol. mass around 20 kDa and neutral optimum pH (7.0-7.5). It requires Mg²⁺ and preferentially hydrolyzes substrates with four phosphate groups. Km for .epsilon.-(Ap4A) is 1.3 .mu.M and Ki for Ap4A and Gp4G are 1 and 0.2 .mu.M resp. Km for Ap4A detd. by HPLC is 1.6 .mu.M. .epsilon.-(Ap5A) and .epsilon.-(Ap6A) are hydrolyzed at reduced rates. This enzyme is inhibited by Zn²⁺, F⁻ and very strongly by Ap4 and .epsilon.-Ap4. Ca²⁺ cannot replace Mg²⁺, but behaves as inhibitor in its presence. The substrate analogs dinucleoside triphosphates Ap3A, Gp3G, m7Gp3G and m7Gp3A and the periodate-oxidized nucleotides o-(Ap4A), o.epsilon.-(Ap4A), o-Ap4 and o.epsilon.-Ap4 behave as inhibitors. Ap3Aase exhibits a mol. mass around 30 kDa and neutral optimum pH (7.0-7.5). It requires Mg²⁺ or Ca²⁺, but retains a low measurable activity around 10% in the absence of these divalent cations. It only hydrolyzes substrates with three phosphate groups. Km for .epsilon.-(Ap3A) is 11 .mu.M and Ki for Ap3A and Gp3G are 20 and 22 .mu.M, resp. Km for Ap3A detd. by HPLC is 16 .mu.M. m7Gp3G and m7Gp3A are also good substrates for triphosphatase.

L13 ANSWER 44 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 170136-15-9 REGISTRY

CN DNA, d(T-T-T-T-T-T-T-T-T-T-T), complex with stereoisomer of 2-[(6-amino-9H-purin-9-yl)methoxy]-1,3-propanediol hydrogen phosphate (12:11) (ester) (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,3-Propanediol, 2-[(6-amino-9H-purin-9-yl)methoxy]-, stereoisomer, hydrogen phosphate (12:11) (ester), complex with DNA d(T-T-T-T-T-T-T-T-T-T-T-T) (1:1) (9CI)

CN Deoxyribonucleic acid, d(T-T-T-T-T-T-T-T-T-T-T-T), complex with stereoisomer of 2-[(6-amino-9H-purin-9-yl)methoxy]-1,3-propanediol hydrogen phosphate (12:11) (ester) (1:1)

FS NUCLEIC ACID SEQUENCE; STEREOSEARCH

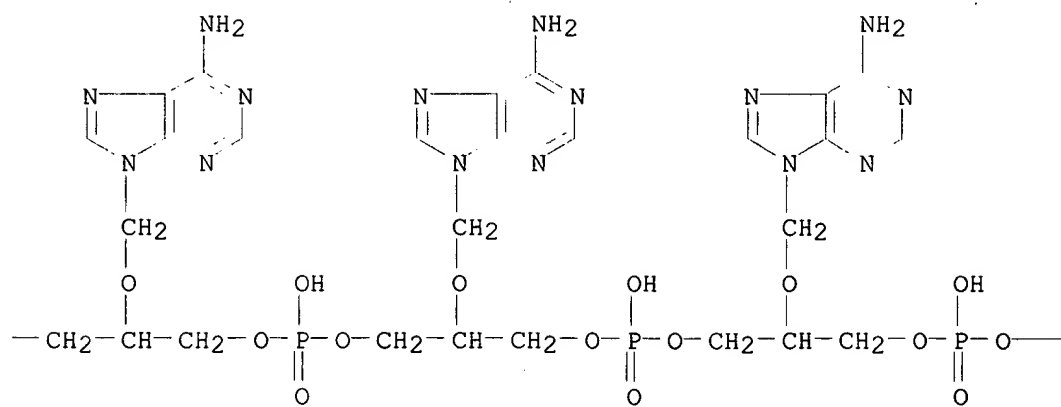
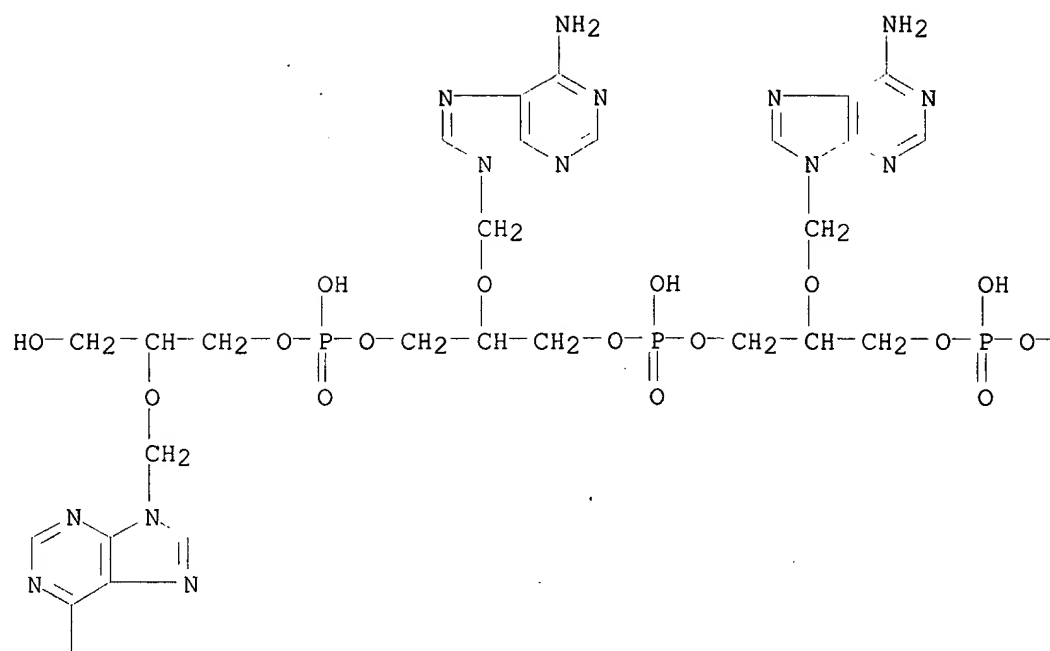
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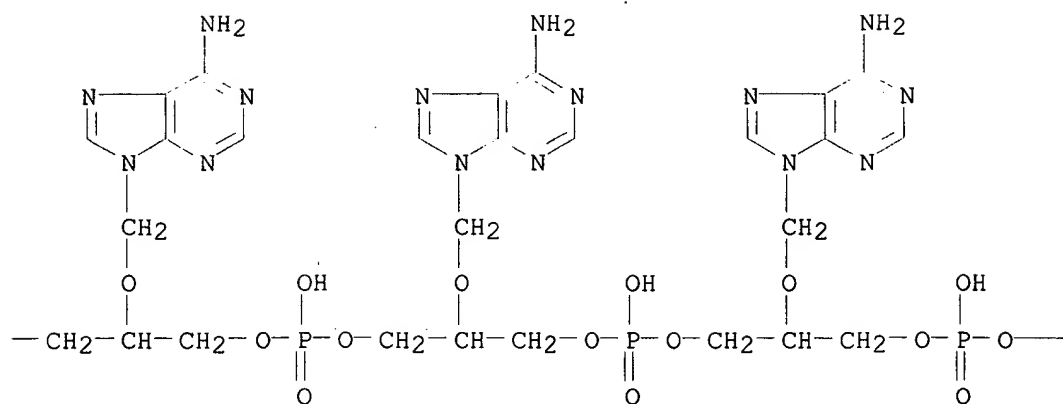
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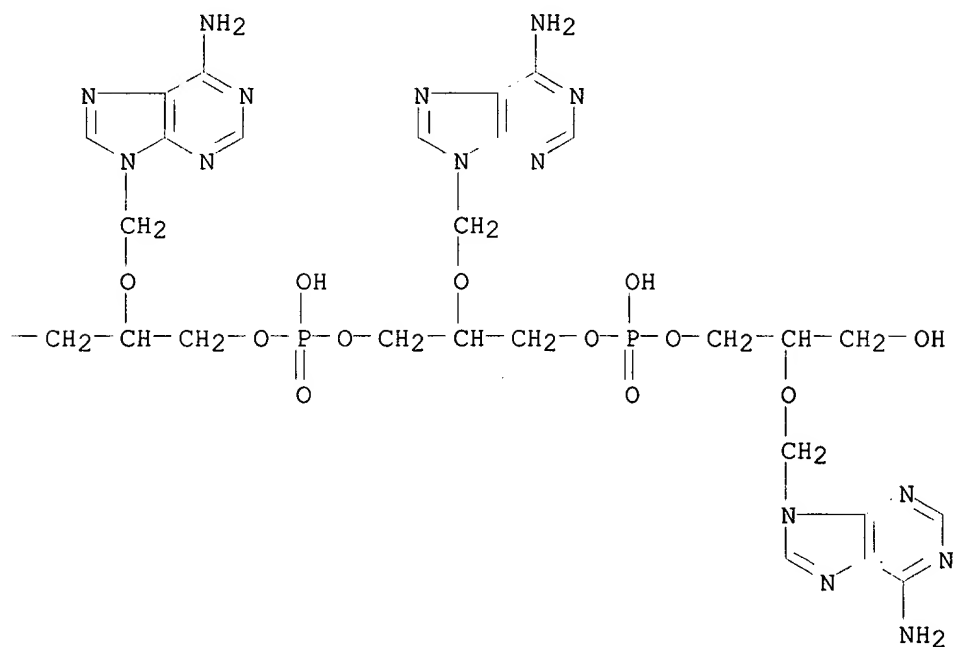
CMF C108 H145 N60 O58 P11



PAGE 1-C



PAGE 1-D



PAGE 2-A

NH₂

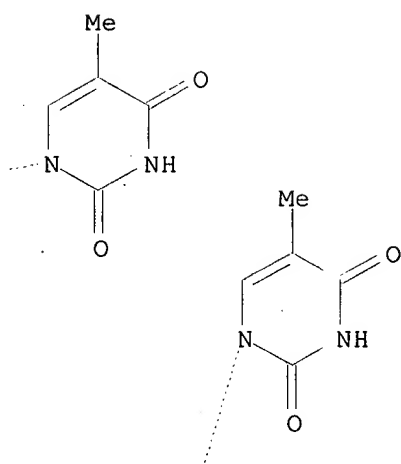
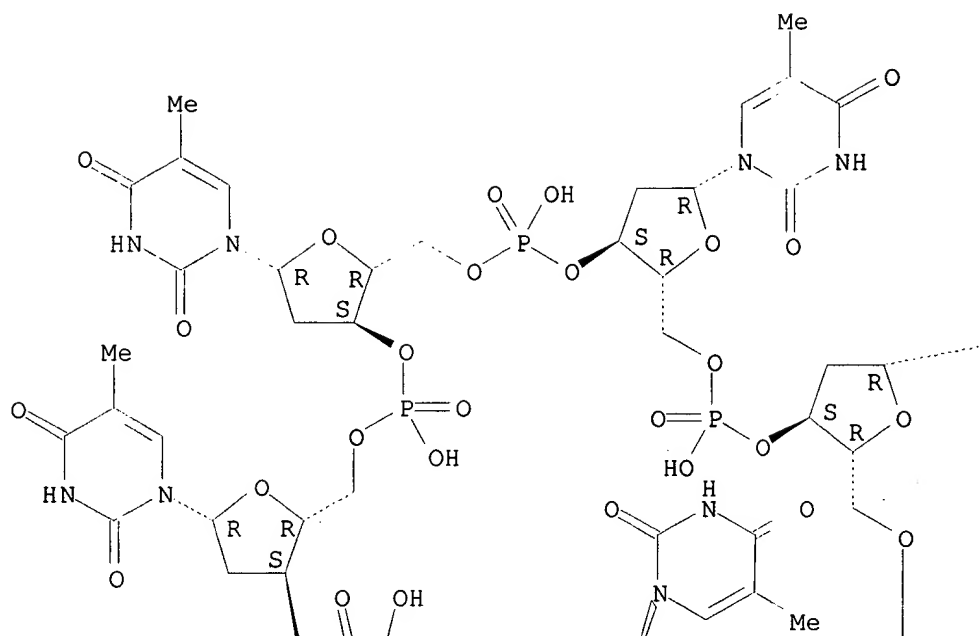
CM 2

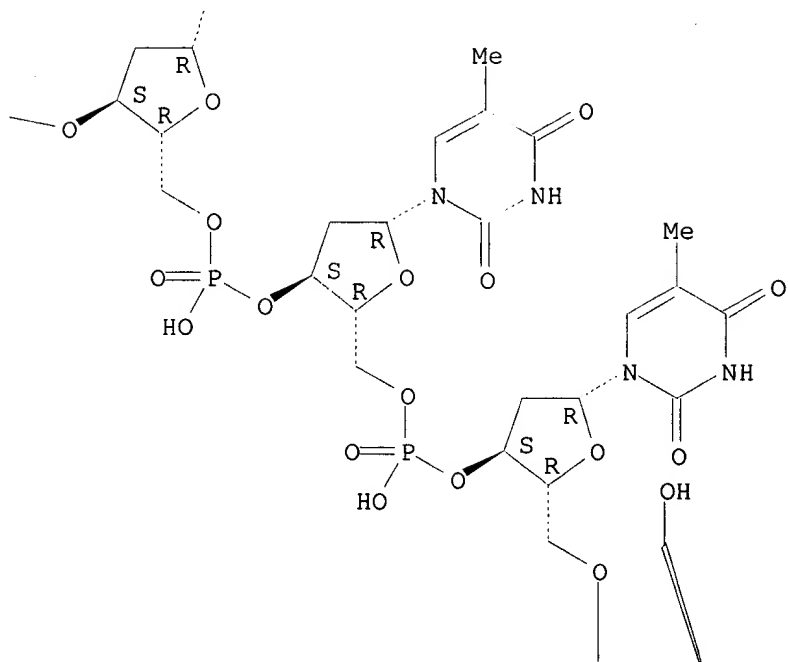
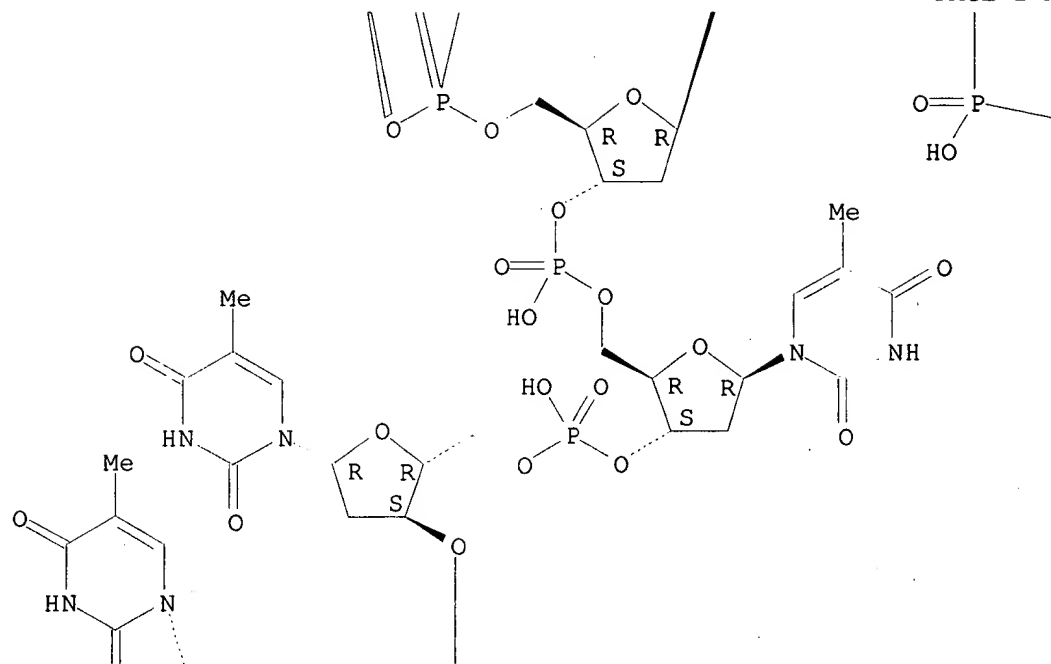
CRN 57777-82-9

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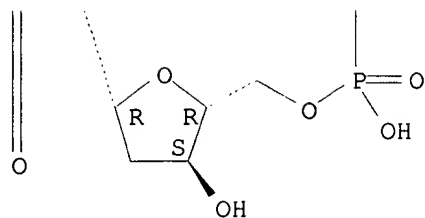
Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16

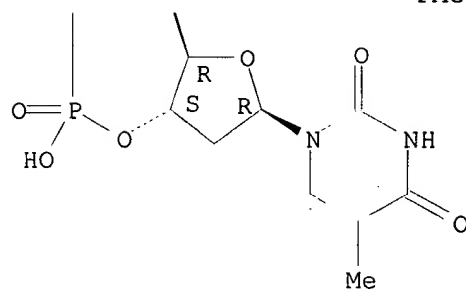




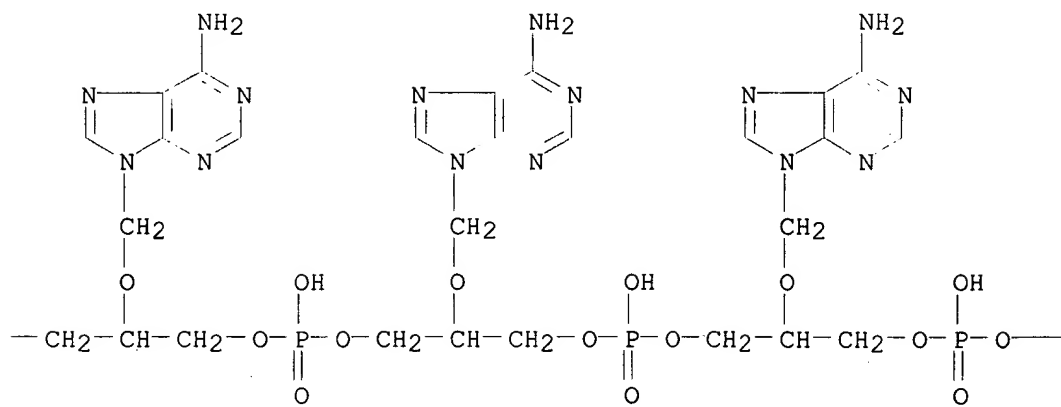
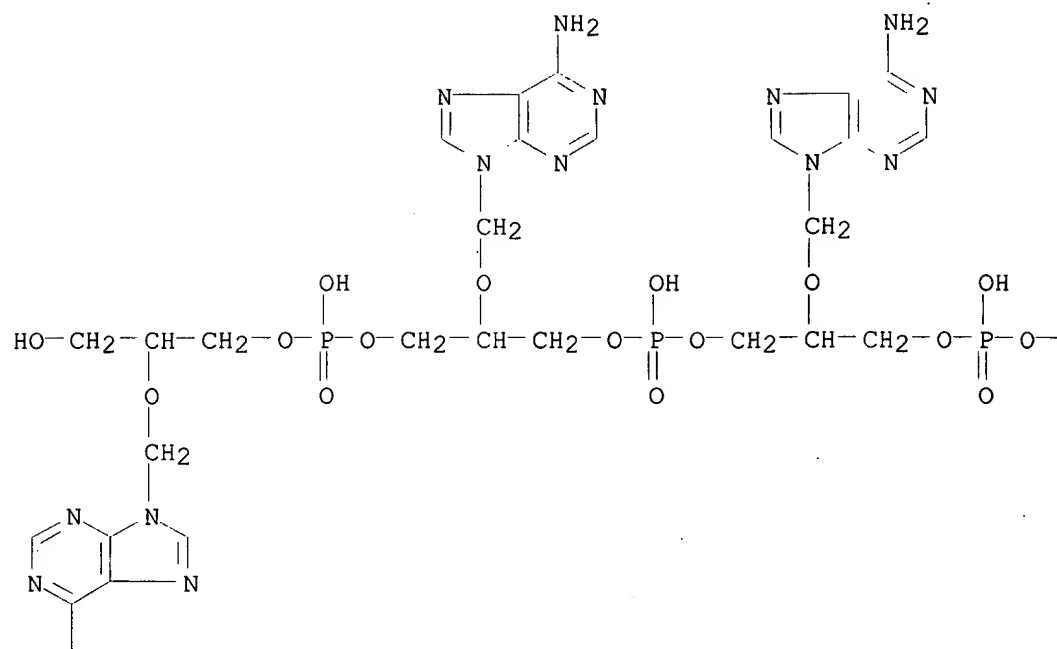
PAGE 3-A



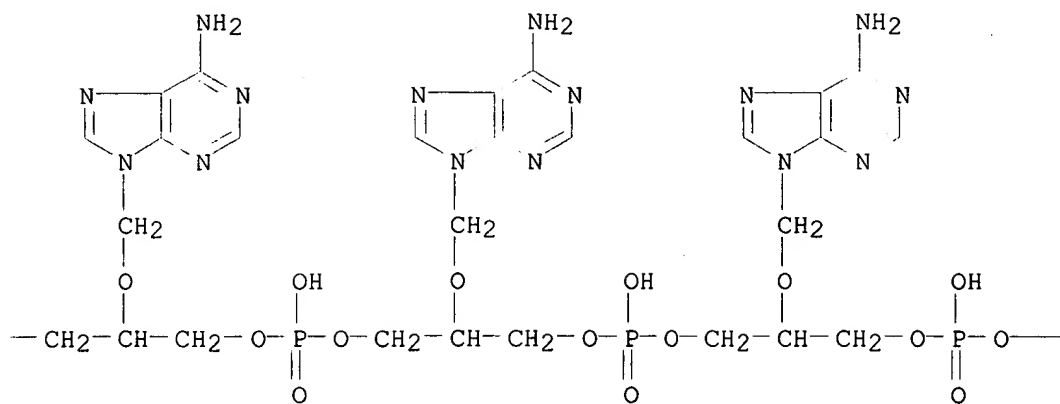
PAGE 3-B



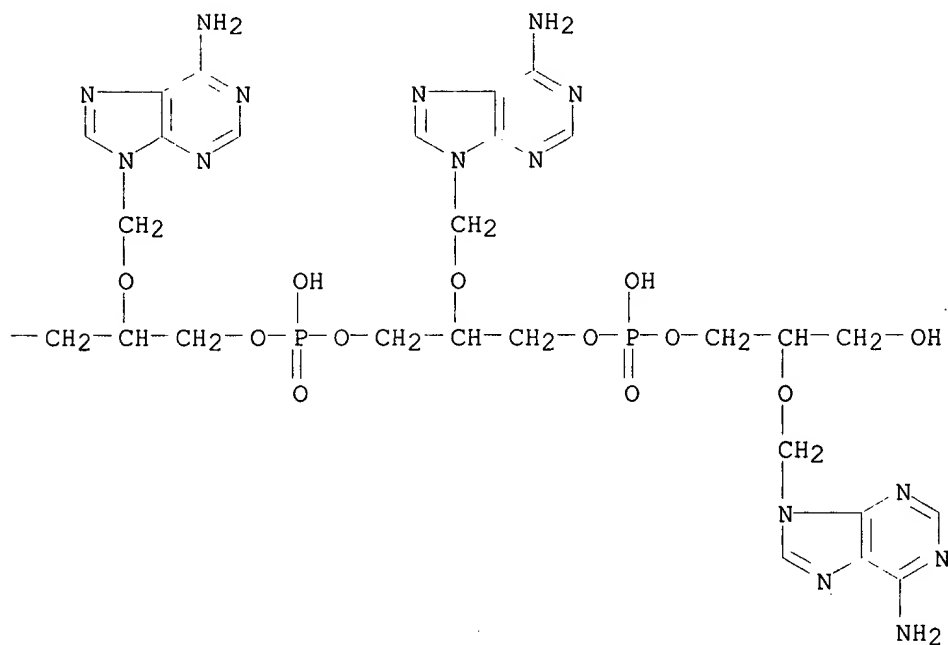
L13 ANSWER 45 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 169932-34-7 REGISTRY
CN 1,3-Propanediol, 2-[(6-amino-9H-purin-9-yl)methoxy]-, hydrogen phosphate
(12:11) (ester), stereoisomer (9CI) (CA INDEX NAME)
MF C108 H145 N60 O58 P11
CI COM
SR CA



PAGE 1-C



PAGE 1-D



PAGE 2-A

NH₂

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L13 ANSWER 46 OF 166 REGISTRY COPYRIGHT 2002 ACS

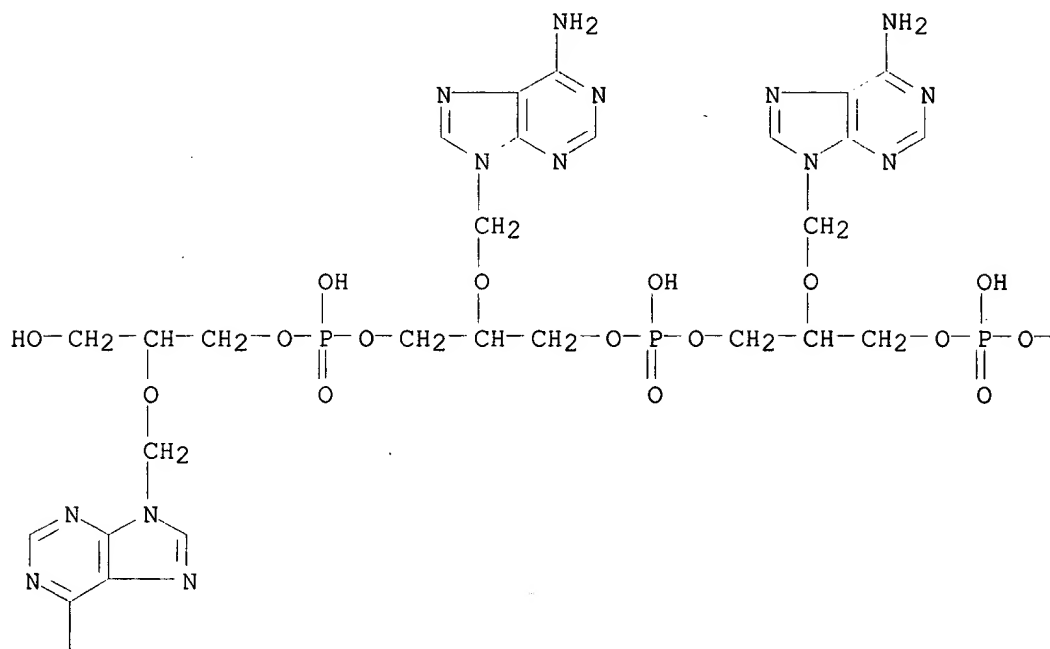
RN 169874-08-2 REGISTRY

CN 1,3-Propanediol, 2-[(6-amino-9H-purin-9-yl)methoxy]-, dihydrogen phosphate (ester) hydrogen phosphate (ester) (12:1:11), stereoisomer (9CI) (CA

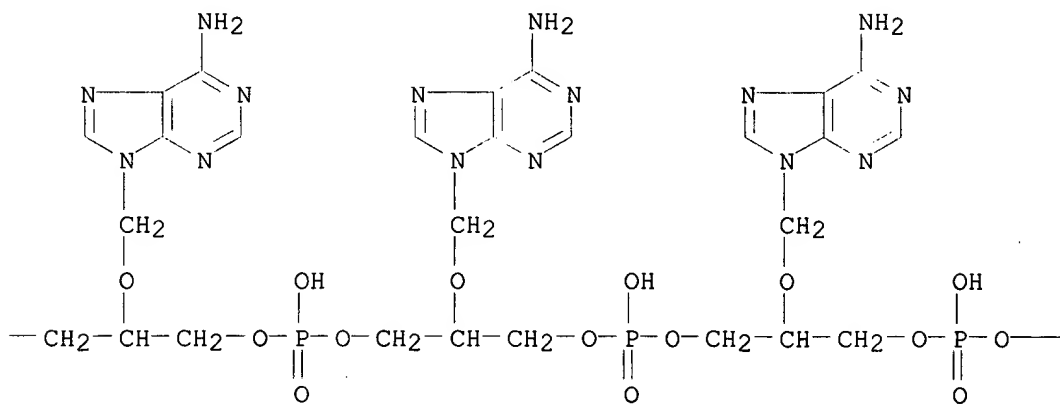
Searched by: Mary Hale 308-4258 CM-1 12D16

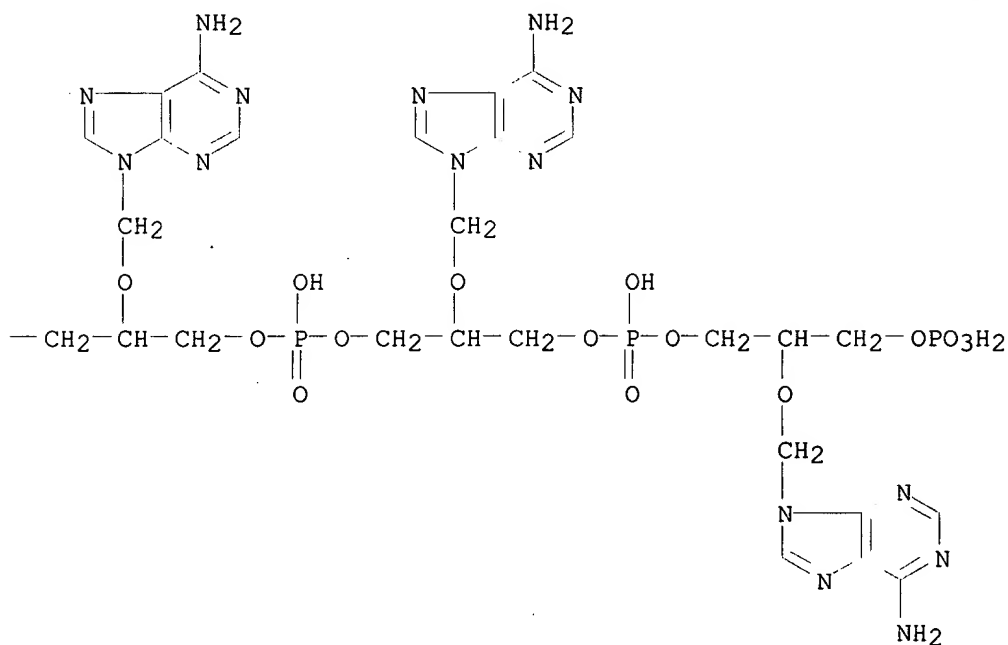
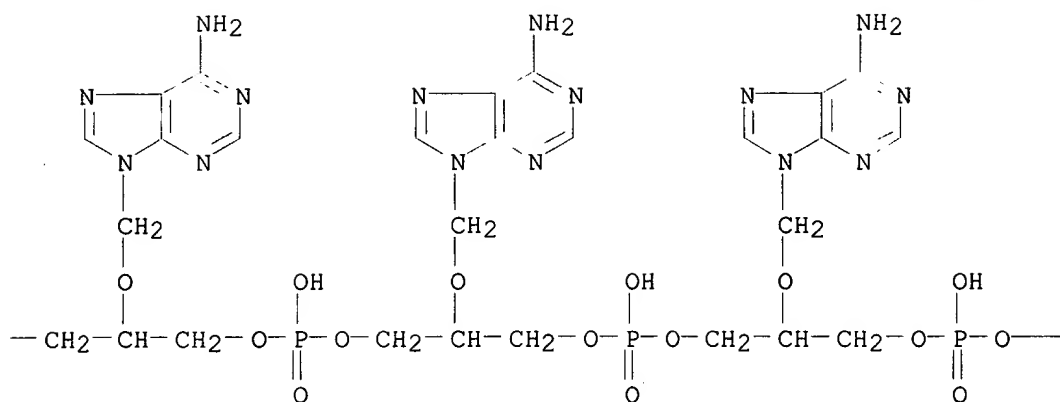
INDEX NAME)
 FS NUCLEIC ACID SEQUENCE
 DR 172840-96-9
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 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A



PAGE 1-B



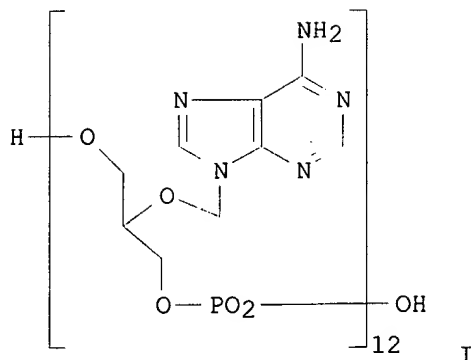


NH₂

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

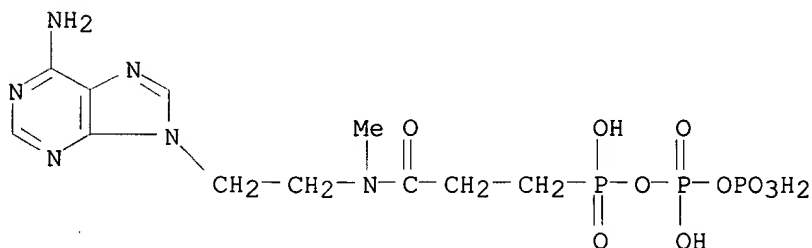
REFERENCE 1: 124:317733 Acyclic oligonucleotide analogs. Merle, Yves; Bonneil, Eric; Merle, Liliane; Sagi, Janos; Szemzo, Attila (Faculte Sciences Rouen, Mont-Saint-Aignan, F-76821, Fr.). Int. J. Biol. Macromol., 17(5), 239-46 (English) 1995. CODEN: IJBMDR. ISSN: 0141-8130.
GI

Searched by: Mary Hale 308-4258 CM-1 12D16



AB (GlyA)12 (I), (GlyA-dT)10 and GlyT-(GlyA-GlyT)9 were synthesized to study their thermal melting, their stability against snake venom phosphodiesterase and their primer/template properties using the Klenow fragment of the Escherichia coli DNA polymerase I enzyme. (GlyA)12 hybridized to dodecathymidylate p(dT)12, and the complex presented a sharp melting with a T_m at 24.degree.C. This assocn. was confirmed by CD curves which were similar to those of the natural oligonucleotide duplexes in A-conformation. (GlyA)12 proved very stable against snake venom phosphodiesterase hydrolysis. The reaction rate was more than 10,000 times slower than that of p(dT)12. (GlyA)12 served as a primer for the Klenow DNA polymerase. When (GlyA)12 was complexed with the poly(dT) template, the enzyme polymd. dATP but the reaction was much slower than with the (GlyT)12 primer. Mol. modeling of atactic (GlyA)12.cntdot.(dT)12 of the A-conformation indicates that this conformation is energetically possible.

L13 ANSWER 47 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 168696-40-0 REGISTRY
 CN Diphosphoric acid, monoanhydride with [3-[[2-(6-amino-9H-purin-9-yl)ethyl]methylamino]-3-oxopropyl]phosphonic acid (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C11 H19 N6 O10 P3
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:257211 Acyclic nucleoside and nucleotide analogs with amide

Searched by: Mary Hale 308-4258 CM-1 12D16

bond. Efimtseva, E. V.; Mikhailov, S. N.; Jasko, M. V.; Malakhov, D. V.; Semizarov, D. G.; Fomicheva, M. V.; Kern, E. R. (Engelhardt Institute Molecular Biology, Russian Academy Science, Moscow, 117984, Russia). Nucleosides Nucleotides, 14(3-5), 373-5 (English) 1995. CODEN: NUNUD5. ISSN: 0732-8311.

AB A series of acyclic nucleosides and related .alpha.-phosphonyl acyclic analogs of dNTP with an amide bond have been prepd. Their antiviral and cytotoxicity were investigated (no data).

L13 ANSWER 48 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 168696-39-7 REGISTRY

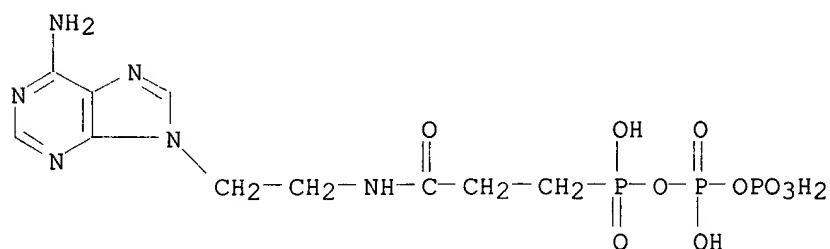
CN Diphosphoric acid, monoanhydride with [3-[[2-(6-amino-9H-purin-9-yl)ethyl]amino]-3-oxopropyl]phosphonic acid (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C10 H17 N6 O10 P3

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:262956 Synthesis and biochemical properties of phosphonyl acyclic analogs of 2'-deoxyadenosine nucleotides. Malakhov, D. V.; Semizarov, D. G.; Yas'ko, M. V. (Engelhardt Inst. Mol. Biol., Russ. Acad. Sci., Moscow, 117984, Russia). Bioorg. Khim., 21(7), 539-544 (Russian) 1995. CODEN: BIKHD7. ISSN: 0132-3423. Publisher: MAIK Nauka.

AB 9-[2-(Phosphonomethylcarbonylamino)ethyl]adenine, 9-[(2-phosphonoethyl)aminocarbonylmethyl]adenine, 9-{2-[(2-phosphonoethyl)carbonylamino]ethyl}adenine and their diphosphates were synthesized. All three diphosphates were shown to incorporate into the 3'-terminus of the DNA chain during the synthesis of the avian myeloblastose virus catalyzed by reverse transcriptase. However, they do not serve as substrates for DNA polymerase .alpha. from human placenta, polymerase .beta. from calf thymus, or terminal deoxynucleotidyl transferase from calf thymus.

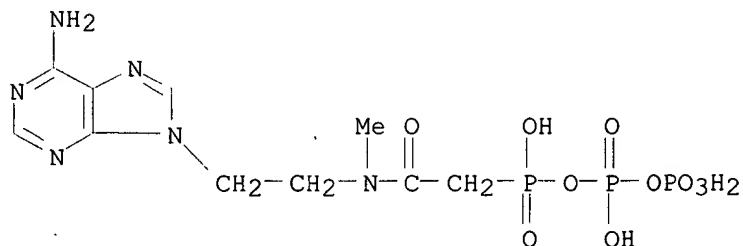
REFERENCE 2: 123:257211 Acyclic nucleoside and nucleotide analogs with amide bond. Efimtseva, E. V.; Mikhailov, S. N.; Jasko, M. V.; Malakhov, D. V.; Semizarov, D. G.; Fomicheva, M. V.; Kern, E. R. (Engelhardt Institute Molecular Biology, Russian Academy Science, Moscow, 117984, Russia). Nucleosides Nucleotides, 14(3-5), 373-5 (English) 1995. CODEN: NUNUD5. ISSN: 0732-8311.

AB A series of acyclic nucleosides and related .alpha.-phosphonyl acyclic analogs of dNTP with an amide bond have been prepd. Their antiviral and cytotoxicity were investigated (no data).

L13 ANSWER 49 OF 166 REGISTRY COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 12D16

RN 168696-38-6 REGISTRY
 CN Diphosphoric acid, monoanhydride with [2-[[2-(6-amino-9H-purin-9-yl)ethyl]methylamino]-2-oxoethyl]phosphonic acid (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C10 H17 N6 O10 P3
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

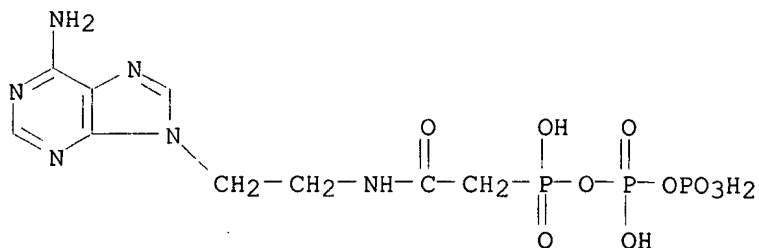
1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:257211 Acyclic nucleoside and nucleotide analogs with amide bond. Efimtseva, E. V.; Mikhailov, S. N.; Jasko, M. V.; Malakhov, D. V.; Semizarov, D. G.; Fomicheva, M. V.; Kern, E. R. (Engelhardt Institute Molecular Biology, Russian Academy Science, Moscow, 117984, Russia). Nucleosides Nucleotides, 14(3-5), 373-5 (English) 1995. CODEN: NUNUD5. ISSN: 0732-8311.

AB A series of acyclic nucleosides and related .alpha.-phosphonyl acyclic analogs of dNTP with an amide bond have been prepd. Their antiviral and cytotoxicity were investigated (no data).

L13 ANSWER 50 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 168696-37-5 REGISTRY
 CN Diphosphoric acid, monoanhydride with [2-[[2-(6-amino-9H-purin-9-yl)ethyl]amino]-2-oxoethyl]phosphonic acid (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C9 H15 N6 O10 P3
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

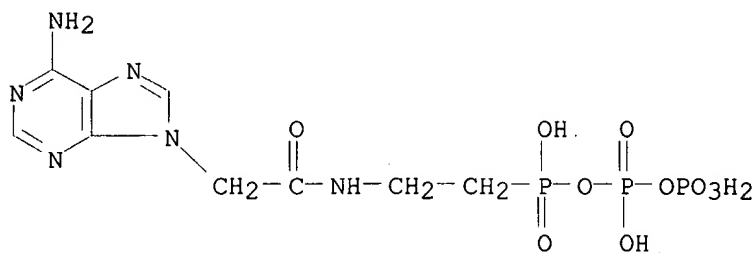
REFERENCE 1: 127:262956 Synthesis and biochemical properties of phosphonyl acyclic analogs of 2'-deoxyadenosine nucleotides. Malakhov, D. V.; Semizarov, D. G.; Yas'ko, M. V. (Engelhardt Inst. Mol. Biol., Russ. Acad. Sci., Moscow, 117984, Russia). Bioorg. Khim., 21(7), 539-544 (Russian) 1995. CODEN: BIKHD7. ISSN: 0132-3423. Publisher: MAIK Nauka.

AB 9-[2-(Phosphonomethylcarbonylamino)ethyl]adenine, 9-[(2-phosphonoethyl)aminocarbonylmethyl]adenine, 9-[2-[(2-phosphonoethyl)carbonylamino]ethyl]adenine and their diphosphates were synthesized. All three diphosphates were shown to incorporate into the 3'-terminus of the DNA chain during the synthesis of the avian myeloblastose virus catalyzed by reverse transcriptase. However, they do not serve as substrates for DNA polymerase .alpha. from human placenta, polymerase .beta. from calf thymus, or terminal deoxynucleotidyl transferase from calf thymus.

REFERENCE 2: 123:257211 Acyclic nucleoside and nucleotide analogs with amide bond. Efimtseva, E. V.; Mikhailov, S. N.; Jasko, M. V.; Malakhov, D. V.; Semizarov, D. G.; Fomicheva, M. V.; Kern, E. R. (Engelhardt Institute Molecular Biology, Russian Academy Science, Moscow, 117984, Russia). Nucleosides Nucleotides, 14(3-5), 373-5 (English) 1995. CODEN: NUNUD5. ISSN: 0732-8311.

AB A series of acyclic nucleosides and related .alpha.-phosphonyl acyclic analogs of dNTP with an amide bond have been prepd. Their antiviral and and cytotoxicity were investigated (no data).

L13 ANSWER 51 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 168696-32-0 REGISTRY
 CN Diphosphoric acid, monoanhydride with [2-[[[6-amino-9H-purin-9-yl)acetyl]amino]ethyl]phosphonic acid (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C9 H15 N6 O10 P3
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:262956 Synthesis and biochemical properties of phosphonyl acyclic analogs of 2'-deoxyadenosine nucleotides. Malakhov, D. V.; Semizarov, D. G.; Yas'ko, M. V. (Engelhardt Inst. Mol. Biol., Russ. Acad. Sci., Moscow, 117984, Russia). Bioorg. Khim., 21(7), 539-544 (Russian) 1995. CODEN: BIKHD7. ISSN: 0132-3423. Publisher: MAIK Nauka.

AB 9-[2-(Phosphonomethylcarbonylamino)ethyl]adenine, 9-[(2-phosphonoethyl)aminocarbonylmethyl]adenine, 9-[2-[(2-phosphonoethyl)carbonylamino]ethyl]adenine and their diphosphates were synthesized. All three diphosphates were shown to incorporate into the

3'-terminus of the DNA chain during the synthesis of the avian myeloblastose virus catalyzed by reverse transcriptase. However, they do not serve as substrates for DNA polymerase .alpha. from human placenta, polymerase .beta. from calf thymus, or terminal deoxynucleotidyl transferase from calf thymus.

REFERENCE 2: 123:257211 Acyclic nucleoside and nucleotide analogs with amide bond. Efimtseva, E. V.; Mikhailov, S. N.; Jasko, M. V.; Malakhov, D. V.; Semizarov, D. G.; Fomicheva, M. V.; Kern, E. R. (Engelhardt Institute Molecular Biology, Russian Academy Science, Moscow, 117984, Russia). Nucleosides Nucleotides, 14(3-5), 373-5 (English) 1995. CODEN: NUNUD5. ISSN: 0732-8311.

AB A series of acyclic nucleosides and related .alpha.-phosphonyl acyclic analogs of dNTP with an amide bond have been prepd. Their antiviral and cytotoxicity were investigated (no data).

L13 ANSWER 52 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 166403-67-4 REGISTRY

CN Diphosphoric acid, monoanhydride with [[2-(2,6-diamino-9H-purin-9-yl)-1-methylethoxy]methyl]phosphonic acid, (R)- (9CI) (CA INDEX NAME)

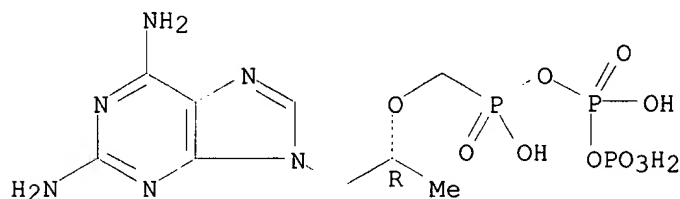
FS STEREOSEARCH

MF C9 H17 N6 O10 P3

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:44484 Incorporation of selected nucleoside phosphonates and anti-human immunodeficiency virus nucleotide analogs into DNA by human DNA polymerases .alpha., .beta. and .gamma.. Cihlar, T.; Chen, M. S. (Gilead Sciences, Foster City, CA, 94404, USA). Antiviral Chemistry & Chemotherapy, 8(3), 187-195 (English) 1997. CODEN: ACCHEH. ISSN: 0956-3202. Publisher: International Medical Press.

AB Incorporation of selected diphosphates of nucleoside phosphonates and triphosphates of currently approved anti-human immunodeficiency virus nucleoside analogs into DNA by human DNA polymerases .alpha., .beta. and .gamma. was studied. All three polymerases were able to incorporate diphosphates of 9-(2-phosphonomethoxyethyl)adenine (PMEApp), 9-(2-phosphonomethoxyethyl)guanine (PMEGpp), (R)-9-(2-phosphonomethoxypropyl)adenine (PMPApp), (R)-9-(2-phosphonomethoxypropyl)-2,6-diaminopurine (PMPDApp) and (2R,5R)-9-[2,5-dihydro-5-(phosphonomethoxy)-2-furanyl]adenine (D4AApp) into primer/template DNA of defined sequence. After incorporation, these nucleoside phosphonates acted as terminators of primer extension. Kinetic consts. of their incorporation were detd. and compared with those for incorporation of ddATP, ddCTP, (-)-2'-deoxy-3'-thiacytidine triphosphate (3TC-TP), 2',3'-didehydro-3'-deoxythymidine triphosphate (d4T-TP) and

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3'-azido-3'-deoxythymidine triphosphate (AZT-TP). Relative efficiencies of incorporation (percentage of the incorporation efficiency for the corresponding natural deoxynucleoside triphosphate) by DNA polymerase .alpha. ranged from 0.05% for 3TC-TP to 51% for PMEGpp. DNA polymerase .beta. catalyzed the incorporation with relative efficiencies ranging from 0.014% for AZT-TP to 125% for ddCTP, and efficiencies of incorporation by DNA polymerase .gamma. varied between 0.13% for 3TC-TP and 325% for ddCTP. Generally, the lowest incorporation efficiencies with all three polymerases were found for PMPApp (0.06-1.4%) and PMPDAPpp (0.075-2.2%).

REFERENCE 2: 125:268990 Structural features of acyclic nucleotide analogs conferring inhibitory effects on cellular replicative DNA polymerases. Kramata, Pavel; Birkus, Gabriel; Otmar, Miroslav; Votruba, Ivan; Holy, Antonin (Institute Organic Chemistry Biochemistry, Academy Sciences Czech Republic, Prague, 166 10, Czech Rep.). Collect. Czech. Chem. Commun., 61(Spec. Issue), S188-S191 (English) 1996. CODEN: CCCCAK. ISSN: 0010-0765.

AB Diphosphates of phosphonomethoxyalkyl acyclic nucleotide analogs were tested as inhibitors of two proteolyzed forms of cellular repetitive DNA polymerase .epsilon., and DNA polymerases .alpha. and .delta.. The Ki/Km ratios are given. Effects of different substitutions on their inhibitory activity are discussed.

REFERENCE 3: 123:136923 Kinetic interaction of the diphosphates of 9-(2-phosphonylmethoxyethyl)adenine and other anti-HIV active purine congeners with HIV reverse transcriptase and human DNA polymerases .alpha., .beta. and .gamma.. Cherrington, J. M.; Allen, S. J. W.; Bischofberger, N.; Chen, M. S. (Gilead Sciences, Inc., Foster City, CA, 94404, USA). Antiviral Chem. Chemother., 6(4), 217-21 (English) 1995. CODEN: ACCHEH. ISSN: 0956-3202.

AB The inhibitory effects of the diphosphates of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) and its analogs on HIV reverse transcriptase and human DNA polymerases .alpha., .beta., and .gamma. were studied. The analogs investigated were the diphosphates of 9-(2-phosphonylmethoxypropyl)adenine (PMPApp), 9-(2-phosphonylmethoxypropyl)-2,6-diaminopurine (PMPDAPpp), and (2R,5R)-9-[2,5-dihydro-5-(phosphonylmethoxy)-2-furanyl]adenine (D4APpp). These 4 compds. were much more inhibitory to HIV reverse transcriptase when an RNA template rather than a DNA template was used. The Ki values for the 4 compds. were in the range of 11-22 nM with an RNA template. The Ki values for ddCTP and AZTTP were 54 and 8 nM, resp. PMEApp and its analogs showed varying degrees of inhibition of the human DNA polymerases. The Ki values for PMEApp, PMPApp and PMPDAPpp against DNA polymerase .alpha. were in the micromolar range, whereas D4APpp was a poor inhibitor of this enzyme with a Ki of 65.9 .mu.M. The inhibition of DNA polymerase .beta. by PMEApp, PMPApp and D4APpp was minimal, whereas PMPDAPpp showed higher inhibition of DNA polymerase .beta. with a Ki of 9.71 .mu.M. The Ki values for PMEApp and D4APpp against DNA polymerase .gamma. were submicromolar, whereas PMPApp and PMPDAPpp were much less inhibitory to this enzyme. For comparison, ddCTP was found to be a more potent inhibitor of DNA polymerases .beta. and .gamma. than the diphosphates of PMEApp and its analogs.

L13 ANSWER 53 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 166403-66-3 REGISTRY

CN Diphosphoric acid, monoanhydride with [[(1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)-1-methylethoxy]methyl]phosphonic acid, (R)-

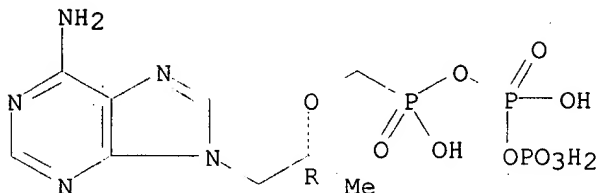
FS STEREOSEARCH

MF C9 H16 N5 O10 P3

Searched by: Mary Hale 308-4258 CM-1 12D16

SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:47907 LC/MS determination of the intracellular concentration of two novel aryl phosphoramidate prodrugs of PMPA and their metabolites in dog PBMC. Lynch, Theresa; Eisenberg, Gene; Kernan, Michael (Gilead Sciences, Foster City, CA, 94404, USA). Nucleosides, Nucleotides & Nucleic Acids, 20(4-7), 1415-1419 (English) 2001. CODEN: NNNAFY. ISSN: 1525-7770. Publisher: Marcel Dekker, Inc..

AB LC/MS assays were developed to det. the plasma and intracellular concns. of two aryl phosphoramidate prodrugs of the nucleotide analog 9-[2-R-(phosphonomethoxy)propyl]adenine. LC/MS was used to demonstrate the presence of high concns. of PMPA in peripheral blood mononucleocytes following oral administration of prodrugs in dogs. High concns. of PMPA and active metabolite were detected in MT-2 cells incubated with prodrug using an ion-pairing LC/MS assay.

REFERENCE 2: 136:148 Metabolism of GS-7340, a novel phenyl monophosphoramidate intracellular prodrug of PMPA, in blood. Eisenberg, Eugene J.; He, Gong-Xin; Lee, William A. (Gilead Sciences, Foster City, CA, USA). Nucleosides, Nucleotides & Nucleic Acids, 20(4-7), 1091-1098 (English) 2001. CODEN: NNNAFY. ISSN: 1525-7770. Publisher: Marcel Dekker, Inc..

AB PMPA, an acyclic nucleoside phosphonate analog, is a potent inhibitor of HIV. In the cells, PMPA is efficiently phosphorylated by intracellular kinases to produce PMPApp, the pharmacol. active metabolite. Despite its demonstrated antiviral potency, PMPA has limited cell permeability presumably resulting from the presence of two neg. charges on the phosphonyl group. To enhance intracellular concns. of PMPA, we developed a prodrug, selectively metabolized inside cells. GS-7340 (9-[(R)-2-[[[(S)-1-(isopropoxycarbonyl)ethyl]amino]phenoxy-phosphinyl]methoxy] propyl]adenine) is a prodrug which is orally bioavailable in dogs as the intact prodrug and has demonstrated anti-HIV activity in cell culture of over 1000-fold greater than that of PMPA. The metab. of PMPA in peripheral blood mononuclear cells (PBMC), red blood cells (RBC) and plasma was examd. following exposure of whole blood to PMPA or GS-7340 at concns. similar to ones obsd. systemically following oral administration in dogs. Following 1 h incubation with whole blood, GS-7340 was stable in plasma, produced high levels of PMPA and its phosphorylated metabolites in PBMC but not in RBC. No intact prodrug was present in PBMC. The only other species present in PBMC was monoalaninyl PMPA. The levels of PMPA and the phosphorylated metabolites were over 20 times greater than those after incubation with PMPA. The dog and human blood data were similar. The intracellular levels of PMPA and PMPApp were roughly proportional to GS-7340 over a 10-fold concn. range indicating a

lack of saturability of uptake and phosphorylation. Since PMPApp is the species responsible for antiviral activity of PMPA, the high intracellular levels of PMPApp should be an important indicator of greater clin. efficacy of GS-7340.

REFERENCE 3: 127:44484 Incorporation of selected nucleoside phosphonates and anti-human immunodeficiency virus nucleotide analogs into DNA by human DNA polymerases .alpha., .beta. and .gamma.. Cihlar, T.; Chen, M. S. (Gilead Sciences, Foster City, CA, 94404, USA). Antiviral Chemistry & Chemotherapy, 8(3), 187-195 (English) 1997. CODEN: ACCHEH. ISSN: 0956-3202. Publisher: International Medical Press.

AB Incorporation of selected diphosphates of nucleoside phosphonates and triphosphates of currently approved anti-human immunodeficiency virus nucleoside analogs into DNA by human DNA polymerases .alpha., .beta. and .gamma. was studied. All three polymerases were able to incorporate diphosphates of 9-(2-phosphonomethoxyethyl)adenine (PMEApp), 9-(2-phosphonomethoxyethyl)guanine (PMEGpp), (R)-9-(2-phosphonomethoxypropyl)adenine (PMPApp), (R)-9-(2-phosphonomethoxypropyl)-2,6-diaminopurine (PMPDAPpp) and (2R,5R)-9-[2,5-dihydro-5-(phosphonomethoxy)-2-furanyl]adenine (D4APpp) into primer/template DNA of defined sequence. After incorporation, these nucleoside phosphonates acted as terminators of primer extension. Kinetic consts. of their incorporation were detd. and compared with those for incorporation of ddATP, ddCTP, (-)-2'-deoxy-3'-thiacytidine triphosphate (3TC-TP), 2',3'-didehydro-3'-deoxythymidine triphosphate (d4T-TP) and 3'-azido-3'-deoxythymidine triphosphate (AZT-TP). Relative efficiencies of incorporation (percentage of the incorporation efficiency for the corresponding natural deoxynucleoside triphosphate) by DNA polymerase .alpha. ranged from 0.05% for 3TC-TP to 51% for PMEGpp. DNA polymerase .beta. catalyzed the incorporation with relative efficiencies ranging from 0.014% for AZT-TP to 125% for ddCTP, and efficiencies of incorporation by DNA polymerase .gamma. varied between 0.13% for 3TC-TP and 325% for ddCTP. Generally, the lowest incorporation efficiencies with all three polymerases were found for PMPApp (0.06-1.4%) and PMPDAPpp (0.075-2.2%).

REFERENCE 4: 125:268990 Structural features of acyclic nucleotide analogs conferring inhibitory effects on cellular replicative DNA polymerases. Kramata, Pavel; Birkus, Gabriel; Otmar, Miroslav; Votruba, Ivan; Holy, Antonin (Institute Organic Chemistry Biochemistry, Academy Sciences Czech Republic, Prague, 166 10, Czech Rep.). Collect. Czech. Chem. Commun., 61(Spec. Issue), S188-S191 (English) 1996. CODEN: CCCCAK. ISSN: 0010-0765.

AB Diphosphates of phosphonomethoxyalkyl acyclic nucleotide analogs were tested as inhibitors of two proteolyzed forms of cellular repetitive DNA polymerase .epsilon., and DNA polymerases .alpha. and .delta.. The Ki/Km ratios are given. Effects of different substitutions on their inhibitory activity are discussed.

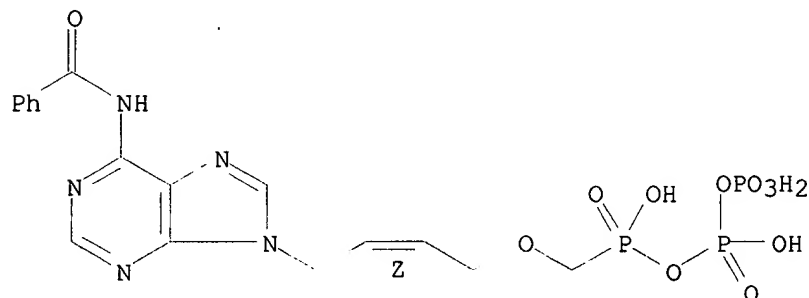
REFERENCE 5: 123:136923 Kinetic interaction of the diphosphates of 9-(2-phosphonylmethoxyethyl)adenine and other anti-HIV active purine congeners with HIV reverse transcriptase and human DNA polymerases .alpha., .beta. and .gamma.. Cherrington, J. M.; Allen, S. J. W.; Bischofberger, N.; Chen, M. S. (Gilead Sciences, Inc., Foster City, CA, 94404, USA). Antiviral Chem. Chemother., 6(4), 217-21 (English) 1995. CODEN: ACCHEH. ISSN: 0956-3202.

AB The inhibitory effects of the diphosphates of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) and its analogs on HIV reverse transcriptase and human DNA polymerases .alpha., .beta., and .gamma. were studied. The analogs investigated were the diphosphates of 9-(2-phosphonylmethoxypropyl)adenine (PMPApp), 9-(2-phosphonylmethoxypropyl)-2,6-diaminopurine (PMPDAPpp), and (2R,5R)-9-[2,5-dihydro-5-(phosphonylmethoxy)-2-furanyl]adenine (D4APpp).

These 4 compds. were much more inhibitory to HIV reverse transcriptase when an RNA template rather than a DNA template was used. The K_i values for the 4 compds. were in the range of 11-22 nM with an RNA template. The K_i values for ddCTP and AZTTP were 54 and 8 nM, resp. PMEApp and its analogs showed varying degrees of inhibition of the human DNA polymerases. The K_i values for PMEApp, PMPApp and PMPDApp against DNA polymerase .alpha. were in the micromolar range, whereas D4App was a poor inhibitor of this enzyme with a K_i of 65.9 .mu.M. The inhibition of DNA polymerase .beta. by PMEApp, PMPApp and D4App was minimal, whereas PMPDApp showed higher inhibition of DNA polymerase .beta. with a K_i of 9.71 .mu.M. The K_i values for PMEApp and D4App against DNA polymerase .gamma. were submicromolar, whereas PMPApp and PMPDApp were much less inhibitory to this enzyme. For comparison, ddCTP was found to be a more potent inhibitor of DNA polymerases .beta. and .gamma. than the diphosphates of PMEA and its analogs.

L13 ANSWER 54 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 164212-13-9 REGISTRY
 CN Triphosphoric acid, P-[[[4-[6-(benzoylamino)-9H-purin-9-yl]-2-butenyl]oxy)methyl] ester, diammonium salt, (Z)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C17 H20 N5 O11 P3 . 2 H3 N
 SR CA
 LC STN Files: CA, CAPLUS

Double bond geometry as shown.



● 2 NH₃

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:170042 Novel Acyclic Nucleotides and Nucleoside 5'-Triphosphates Imitating 2',3'-Dideoxy-2',3'-didehydro nucleotides: Synthesis and Biological Properties. Shirokova, Elena A.; Tarussova, Natalia B.; Shipitsin, Alexander V.; Semizarov, Dmitry G.; Krayevsky, Alexander A. (V. Engelhardt Institute of Molecular Biology, Moscow, 117984, Russia). J. Med. Chem., 37(22), 3739-48 (English) 1994. CODEN: JMCMAR. ISSN: 0022-2623.

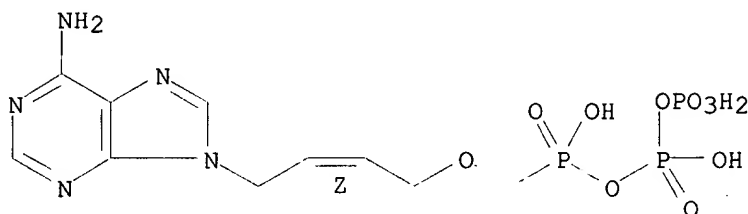
AB A series of pyrophosphoryl (Z)-(phosphonomethoxy)but-2-enyl derivs. of pyrimidines and purines and the corresponding phosphonates were synthesized. The prepd. compds. contain the phosphonate group as an .alpha.-phosphate mimic as well as an acyclic residue emulating the sugar moiety in 2',3'-dideoxy-2',3'-didehydro nucleoside 5'-triphosphates known as highly potent chain terminators of DNA polymerases. Their substrate properties were evaluated in cell-free systems contg. various DNA polymerases including viral reverse transcriptases. These compds.

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manifested good terminating substrate properties toward HIV-1 and AMV reverse transcriptases. They exhibited high selectivity and were not recognized by human DNA polymerases .alpha. and .epsilon., DNA polymerase .beta. from rat liver, Escherichia coli DNA polymerase I, and HSV-1 and CMV DNA polymerases. Phosphonates displayed no activity in HIV-1-infected MT-4 cells cultures; the adenine phosphonate was moderately effective (ED50 = 9 .mu.M).

L13 ANSWER 55 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 164212-07-1 REGISTRY
 CN Diphosphoric acid, monoanhydride with [[[4-(6-amino-9H-purin-9-yl)-2-butenyl]oxy]methyl]phosphonic acid, diammonium salt, (Z)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C10 H16 N5 O10 P3 . 2 H3 N
 SR CA
 LC STN Files: CA, CAPLUS
 CRN (163682-63-1)

Double bond geometry as shown.



● 2 NH3

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:170042 Novel Acyclic Nucleotides and Nucleoside 5'-Triphosphates Imitating 2',3'-Dideoxy-2',3'-didehydro nucleotides: Synthesis and Biological Properties. Shirokova, Elena A.; Tarussova, Natalia B.; Shipitsin, Alexander V.; Semizarov, Dmitry G.; Krayevsky, Alexander A. (V. Engelhardt Institute of Molecular Biology, Moscow, 117984, Russia). J. Med. Chem., 37(22), 3739-48 (English) 1994. CODEN: JMCMAR. ISSN: 0022-2623.

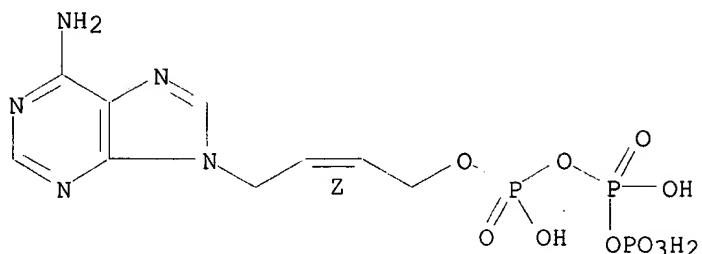
AB A series of pyrophosphoryl (Z)-(phosphonomethoxy)but-2-enyl derivs. of pyrimidines and purines and the corresponding phosphonates were synthesized. The prepd. compds. contain the phosphonate group as an .alpha.-phosphate mimic as well as an acyclic residue emulating the sugar moiety in 2',3'-dideoxy-2',3'-didehydro nucleoside 5'-triphosphates known as highly potent chain terminators of DNA polymerases. Their substrate properties were evaluated in cell-free systems contg. various DNA polymerases including viral reverse transcriptases. These compds. manifested good terminating substrate properties toward HIV-1 and AMV reverse transcriptases. They exhibited high selectivity and were not recognized by human DNA polymerases .alpha. and .epsilon., DNA polymerase .beta. from rat liver, Escherichia coli DNA polymerase I, and HSV-1 and CMV DNA polymerases. Phosphonates displayed no activity in HIV-1-infected MT-4 cells cultures; the adenine phosphonate was moderately effective (ED50 = 9 .mu.M).

L13 ANSWER 56 OF 166 REGISTRY COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 12D16

RN 163682-67-5 REGISTRY
 CN Triphosphoric acid, P-[4-(6-amino-9H-purin-9-yl)-2-butenyl] ester, (Z)-
 (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C9 H14 N5 O10 P3
 SR CA
 LC STN Files: CA, CAPLUS

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

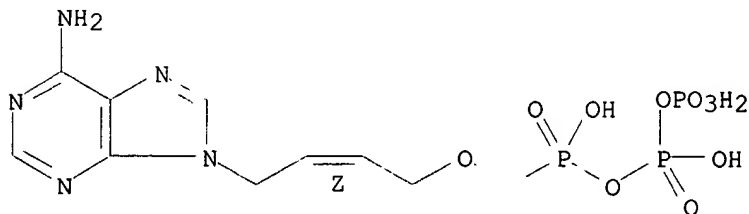
1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:4274 Selectivity of reverse transcriptases. Substrate properties of new acyclic nucleotide analogs. Shirokova, E.; Shipitsin, A.; Semizarov, D. (Engelhardt Inst. Molecular Biology, Russian Academy Sci., Moscow, 117984, Russia). Mol. Biol. (Moscow), 29(2), 461-71 (Russian) 1995. CODEN: MOBIBO. ISSN: 0026-8984.

AB A new series of nucleotide analogs, (Z)-pyrophosphoryl (phosphonyloxymethyl)but-2-enyl derivs. of pyrimidines and purines, were synthesized. Their substrate and inhibitory properties toward some DNA polymerases and reverse transcriptases were evaluated. They were shown to be selective inhibitors of HIV reverse transcriptase. The structure-substrate properties relationships for nucleotide analogs were discussed.

L13 ANSWER 57 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 163682-63-1 REGISTRY
 CN Diphosphoric acid, monoanhydride with [[[4-(6-amino-9H-purin-9-yl)-2-butenyl]oxy]methyl]phosphonic acid, (Z)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C10 H16 N5 O10 P3
 CI COM
 SR CA
 LC STN Files: CA, CAPLUS

Double bond geometry as shown.



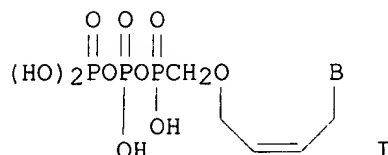
Searched by: Mary Hale 308-4258 CM-1 12D16

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:286474 Novel open-chain nucleotides imitating 2',3'-dideoxy-2',3'-didehydronucleotides: synthesis and substrate properties toward DNA polymerases. Shirokova, E. A.; Tarussova, N. B.; Shipitsin, A. V.; Semizarov, D. G.; Hieber, M.; Krayevsky, A. A. (Engelhardt Inst. of Molecular Biology, Russian Academy of Sciences, Moscow, 117984, Russia). Nucleosides Nucleotides, 14(3-5), 749-51 (English) 1995. CODEN: NUNUD5. ISSN: 0732-8311.

GI



AB Acyclic nucleotide triphosphate isosteres I (B = Ade, Thy, Cyt, Gua) were synthesized and evaluated as potential inhibitors of HIV reverse transcriptases.

REFERENCE 2: 123:4274 Selectivity of reverse transcriptases. Substrate properties of new acyclic nucleotide analogs. Shirokova, E.; Shipitsin, A.; Semizarov, D. (Engelhardt Inst. Molecular Biology, Russian Academy Sci., Moscow, 117984, Russia). Mol. Biol. (Moscow), 29(2), 461-71 (Russian) 1995. CODEN: MOBIBO. ISSN: 0026-8984.

AB A new series of nucleotide analogs, (Z)-pyrophosphoryl (phosphonyloxymethyl)but-2-enyl derivs. of pyrimidines and purines, were synthesized. Their substrate and inhibitory properties toward some DNA polymerases and reverse transcriptases were evaluated. They were shown to be selective inhibitors of HIV reverse transcriptase. The structure-substrate properties relationships for nucleotide analogs were discussed.

L13 ANSWER 58 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 160146-69-0 REGISTRY

CN Triphosphoric acid, P-[5-(6-amino-9H-purin-9-yl)-2-methyl-3-hexenyl] ester, [S-[R*,S*-(Z)]]- (9CI) (CA INDEX NAME)

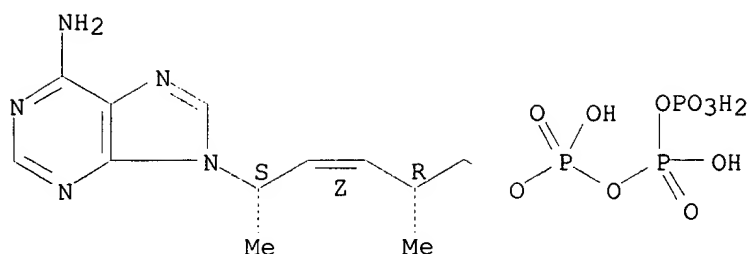
FS STEREOSEARCH

MF C12 H20 N5 O10 P3

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.



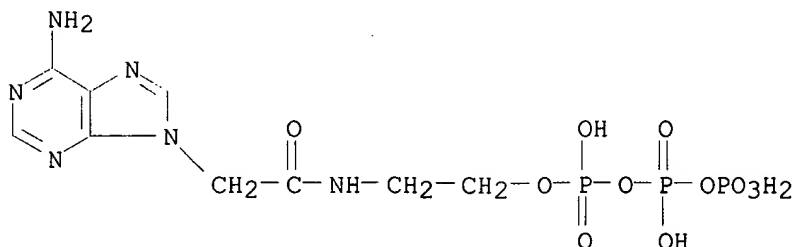
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:73781 Inhibition of DNA synthesis catalyzed by herpes simplex type I DNA polymerase with nucleoside 5'-triphosphates modified at sugar residue or triphosphate group. Kukhanova, M.; Kuznetsova, E.; Jasko, M.; O'Hara, B.; Bekker, J.; Morin, J.; Gluzman, Ya. (Engelhardt Institute of Molecular Biology, Moscow, 117984, Russia). Mol. Biol. (Moscow), 28(4), 875-86 (Russian) 1994. CODEN: MOBIBO. ISSN: 0026-8984.

AB The inhibitory potency of new analogs of nucleoside 5'-triphosphates modified at the sugar residue and or .alpha.-phosphate against herpes simplex virus type 1 DNA polymerase has been evaluated in a cell-free system contg. M13mp10 phage DNA and a synthetic primer. Triphosphates of new acyclic nucleosides [1-(5-hydroxy-2-cis-pentenyl)nucleosides] were the most effective inhibitors among 15 types of nucleoside 5'-triphosphates under investigation, being threefold less active than acyclovirtriphosphate. 5'-Phosphonylmethyl-2'-deoxythymidine .beta.,.gamma.-diphosphate proved to be a poor substrate for DNA polymerase. Compds. with other modifications at .alpha.-phosphate were inactive. Consts. of hydrolysis rate of acyclonucleosides incorporated into the 3' end of primer were detd.

L13 ANSWER 59 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 159141-78-3 REGISTRY
CN Triphosphoric acid, P-[2-[[(6-amino-9H-purin-9-yl)acetyl]amino]ethyl] ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C9 H15 N6 O11 P3
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:295750 Inhibitory analysis of DNA polymerases from human viruses using modified substrates. Kukhanova, M. K.; Kuznetsova, E. V.; Krayevsky, A. A.; O'Hara, B.; Bekker, J.; Morin, J.; Gluzman, Ya. (Engelhardt Inst. Mol. Biol., Moscow, 117984, Russia). Mol. Biol. (Moscow), 28(3), 530-41 (Russian) 1994. CODEN: MOBIBO. ISSN: 0026-8984.

AB A systematic anal. of DNA polymerase of human herpes simplex type 1 virus, cytomegalovirus, and human type 2 adenovirus with the help of a broad set of modified substrates of these enzymes has been carried out. It revealed compds. capable of inhibiting the DNA synthesis catalyzed both by all 3 enzymes and DNA polymerase a from human placenta. Compds. have been found which effectively and specifically inhibit the DNA synthesis catalyzed by some of the above mentioned enzymes. It has been shown that the mol. mechanism of inhibition consists either in the termination of DNA elongation or in inhibition without incorporation into the growing DNA chain.

L13 ANSWER 60 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 148584-28-5 REGISTRY

CN Triphosphoric acid, P-[5-(6-amino-9H-purin-9-yl)-3-pentenyl] ester, (Z)-(9CI) (CA INDEX NAME)

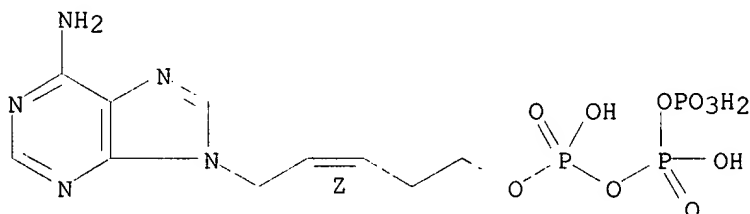
FS STEREOSEARCH

MF C10 H16 N5 O10 P3

SR CA

LC STN Files: CA, CAPLUS

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 119:49826 Synthesis of cis-2-pentene-containing nucleoside analogs and their triphosphates. Mitsner, B. I.; Kochetkova, M. V.; Philippov, D. V.; Tsytoich, A. V.; Dyatkina, N. B. (M.V. Lomonosov Inst. Fine Chem. Technol., Moscow, 117571, Russia). Mol. Biol. (Moscow), 27(1), 174-84 (Russian) 1993. CODEN: MOBIBO. ISSN: 0026-8984.

AB Acyclic analogs of thymidine, adenine, and cytosine, where the ribose moiety is replaced by cis-5-hydroxypentene, were obtained by condensation of cis-5-acetoxy-1-bromo-2-pentene with nucleic acid bases. The triphosphate derivs. of the new nucleosides were also synthesized to evaluate their action as terminators of DNA synthesis catalyzed by DNA polymerases.

L13 ANSWER 61 OF 166 REGISTRY COPYRIGHT 2002 ACS

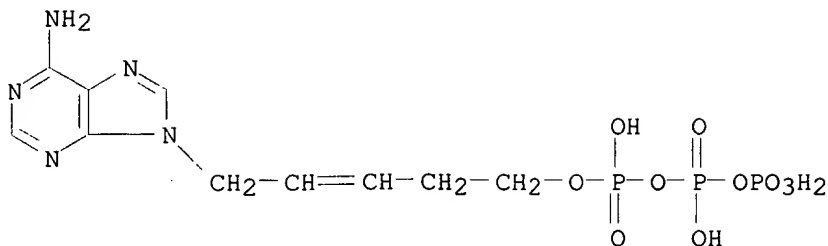
RN 148505-00-4 REGISTRY

CN Triphosphoric acid, P-[5-(6-amino-9H-purin-9-yl)-3-pentenyl] ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

Searched by: Mary Hale 308-4258 CM-1 12D16

MF C10 H16 N5 O10 P3
SR CA
LC STN Files: CA, CAPLUS



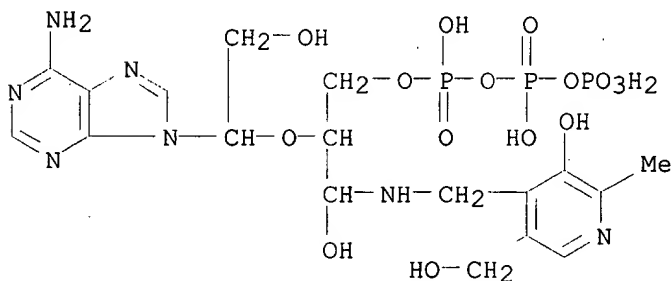
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

- REFERENCE 1: 121:295750 Inhibitory analysis of DNA polymerases from human viruses using modified substrates. Kukhanova, M. K.; Kuznetsova, E. V.; Krayevsky, A. A.; O'Hara, B.; Bekker, J.; Morin, J.; Gluzman, Ya. (Engelhardt Inst. Mol. Biol., Moscow, 117984, Russia). Mol. Biol. (Moscow), 28(3), 530-41 (Russian) 1994. CODEN: MOBIBO. ISSN: 0026-8984.
- AB A systematic anal. of DNA polymerase of human herpes simplex type 1 virus, cytomegalovirus, and human type 2 adenovirus with the help of a broad set of modified substrates of these enzymes has been carried out. It revealed compds. capable of inhibiting the DNA synthesis catalyzed both by all 3 enzymes and DNA polymerase a from human placenta. Compds. have been found which effectively and specifically inhibit the DNA synthesis catalyzed by some of the above mentioned enzymes. It has been shown that the mol. mechanism of inhibition consists either in the termination of DNA elongation or in inhibition without incorporation into the growing DNA chain.
- REFERENCE 2: 119:44000 Acyclic analogs of 2',3'-dideoxy-2',3'-didehydronucleoside 5'-triphosphates as termination substrates of DNA synthesis catalyzed by a range of DNA polymerases. Victorova, L. S.; Mozzherin, D. Ju.; Rosovskaya, T. A.; Kukhanova, M. K.; Krayevsky, A. A. (V. A. Engelhardt Inst. Mol. Biol., Moscow, 117984, Russia). Mol. Biol. (Moscow), 27(1), 143-52 (Russian) 1993. CODEN: MOBIBO. ISSN: 0026-8984.
- AB O-4'-nor-2',3'-deoxy-2',3'-didehydronucleoside 5'-triphosphates are shown to be effective termination substrate of DNA biosynthesis catalyzed by human placental DNA polymerase .alpha. and .epsilon., rat liver DNA polymerase .beta., reverse transcriptase of human immunodeficiency virus and avian myeloblastosis virus, and calf thymus terminal deoxynucleotidyl transferase. These compds. do not interact only with the Escherichia coli DNA polymerase I (Klenow fragment). The probable reasons of interaction of acyclo-d4NTP with the DNA synthesizing complex are discussed.
- REFERENCE 3: 119:43980 Acyclic 2',3'-dideoxy-2',3'-didehydronucleoside 5'-triphosphates as termination substrates of broad set of DNA polymerases. Krayevsky, A. A.; Victorova, L.; Mozzherin, D. Ju.; Kukhanova, M. K. (V. Engelhardt Inst. Mol. Biol., Moscow, 117984, Russia). Nucleosides Nucleotides, 12(1), 83-93 (English) 1993. CODEN: NUNUD5. ISSN: 0732-8311.
- AB O4'-Nor-2',3'-dideoxy-2',3'-didehydronucleoside 5'-triphosphates (acyclo-d4NTP) have been shown to have the properties of effective termination substrates for DNA biosynthesis, catalyzed by several

different DNA polymerases.

L13 ANSWER 62 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 146893-41-6 REGISTRY
CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxy-3-[[[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridinyl]methyl]amino]propyl] ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H28 N7 O15 P3
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

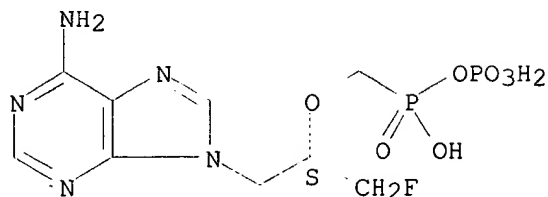
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:164124 Catalytic and structural properties of brain pyridoxal kinase. Choi, Soo Young; Lee, Su Jin; Cho, Sung Woo (Coll. Nat. Sci., Hallym Univ., Chunchon, 200-702, S. Korea). Han'guk Saenghwa Hakhoechi, 25(7), 624-30 (English) 1992. CODEN: KBCJAK. ISSN: 0368-4881.

AB The structure of catalytic domain on pyridoxal kinase purified from pig brain was investigated by using a bifunctional synthetic inhibitor D-ATP-PM and a photoaffinity labeling reagent, N-4-azido-2-nitrophenyl-pyridoxal (NANP). D-ATP-PM is a competitive inhibitor with respect to ATP ($K_i = 3 \mu\text{M}$) and it also behaves as a strong competitive inhibitor respect to pyridoxal ($K_i = 4 \mu\text{M}$). This behavior suggests that D-ATP-PM acts as a bifunctional inhibitor which recognizes both nucleotide and pyridoxal binding site of the kinase. Thus the binding of the binary inhibitor D-ATP-PM may be discussed in ref. to a model which assumes that the two substrate binding sites, located on different domains, are in close proximity. A bulky P-pyridoxamine deriv., N-4-azido-2-nitrophenyl-pyridoxal (NANP) recognizes the binding site of pyridoxal moiety of the enzyme. Upon illumination, the arylazide of NANP acts as an efficient photolabeling reagent of the kinase. A characteristic feature of the photolabeling reagent, which has ability to recognize the substrate binding site, can be exploited to ascertain the chem. nature of amino acid residues at the catalytic domain.

L13 ANSWER 63 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 145986-71-6 REGISTRY
CN Isohypophosphoric acid, [[2-(6-amino-9H-purin-9-yl)-1-(fluoromethyl)ethoxy]methyl]-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C9 H14 F N5 O7 P2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:93736 Phosphorylation of 9-(2-phosphonomethoxyethyl)adenine and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine by AMP(dAMP) kinase from L1210 cells. Merta, Ales; Votruba, Ivan; Jindrich, Jindrich; Holy, Antonin; Cihlar, Tomas; Rosenberg, Ivan; Otmar, Miroslav; Herve, Tchaou Y. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Biochem. Pharmacol., 44(10), 2067-77 (English) 1992. CODEN: BCPCA6. ISSN: 0006-2952.

AB The acyclic nucleotide analogs 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), which display potent antiviral activity, are transformed in the cells to their mono- and diphosphoryl derivs. The enzyme that in 2 steps phosphorylates PMEA and HPMPA to their diphosphoryl derivs. was purified from mouse L1210 cells. The enzyme co-purified with AMP (dAMP) kinase activity; the best substrates of this enzyme were AMP, ADP, and dAMP. Other nucleoside 5'-triphosphates or creatine phosphate could not be substituted for ATP as a phosphate donor. At least one other enzyme (creatine kinase) can transform the monophosphoryl derivs. of the studied compds. to their resp. diphosphates.

L13 ANSWER 64 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 145986-70-5 REGISTRY

CN Isohypophosphoric acid, [[2-(6-amino-9H-purin-9-yl)-1-(fluoromethyl)ethoxy]methyl]-, (R)- (9CI) (CA INDEX NAME)

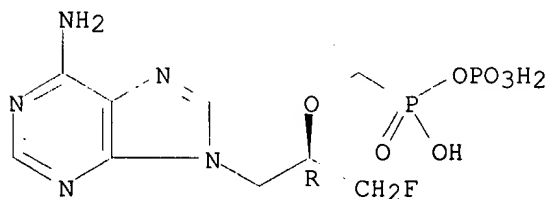
FS STEREOSEARCH

MF C9 H14 F N5 O7 P2

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

REFERENCE 1: 118:93736 Phosphorylation of 9-(2-phosphonomethoxyethyl)adenine and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine by AMP(dAMP) kinase from L1210 cells. Merta, Ales; Votruba, Ivan; Jindrich, Jindrich; Holy, Antonin; Cihlar, Tomas; Rosenberg, Ivan; Otmar, Miroslav; Herve, Tchaou Y. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Biochem. Pharmacol., 44(10), 2067-77 (English) 1992. CODEN: BCPCA6. ISSN: 0006-2952.

AB The acyclic nucleotide analogs 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), which display potent antiviral activity, are transformed in the cells to their mono- and diphosphoryl derivs. The enzyme that in 2 steps phosphorylates PMEA and HPMPA to their diphosphoryl derivs. was purified from mouse L1210 cells. The enzyme co-purified with AMP (dAMP) kinase activity; the best substrates of this enzyme were AMP, ADP, and dAMP. Other nucleoside 5'-triphosphates or creatine phosphate could not be substituted for ATP as a phosphate donor. At least one other enzyme (creatine kinase) can transform the monophosphoryl derivs. of the studied compds. to their resp. diphosphates.

L13 ANSWER 65 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 145899-94-1 REGISTRY

CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)-1-(fluoromethyl)ethoxy]methyl]phosphonic acid, (S)- (9CI) (CA INDEX NAME)

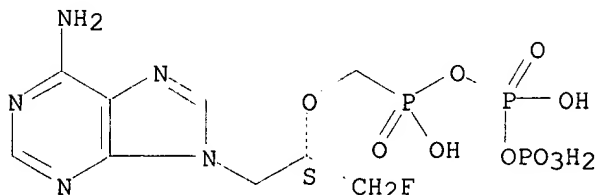
FS STEREOSEARCH

MF C9 H15 F N5 O10 P3

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:93736 Phosphorylation of 9-(2-phosphonomethoxyethyl)adenine and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine by AMP(dAMP) kinase from L1210 cells. Merta, Ales; Votruba, Ivan; Jindrich, Jindrich; Holy, Antonin; Cihlar, Tomas; Rosenberg, Ivan; Otmar, Miroslav; Herve, Tchaou Y. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Biochem. Pharmacol., 44(10), 2067-77 (English) 1992. CODEN: BCPCA6. ISSN: 0006-2952.

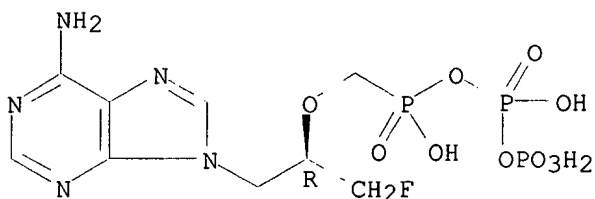
AB The acyclic nucleotide analogs 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), which display potent antiviral activity, are transformed in the cells to their mono- and diphosphoryl derivs. The enzyme that in 2 steps phosphorylates PMEA and HPMPA to their diphosphoryl derivs. was purified from mouse L1210 cells. The enzyme co-purified with AMP (dAMP) kinase activity; the best substrates of this enzyme were AMP, ADP, and dAMP. Other nucleoside 5'-triphosphates or creatine phosphate could not be substituted for ATP as a phosphate donor. At least one other enzyme (creatine kinase) can transform the monophosphoryl derivs. of the studied compds. to their resp.

Searched by: Mary Hale 308-4258 CM-1 12D16

diphosphates.

L13 ANSWER 66 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 145899-93-0 REGISTRY
CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)-1-(fluoromethyl)ethoxy]methyl]phosphonic acid, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C9 H15 F N5 O10 P3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

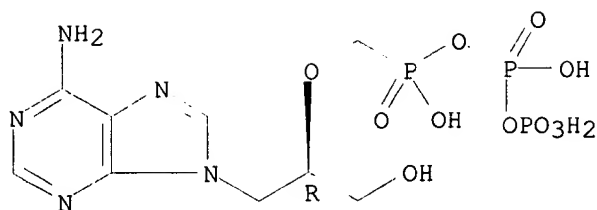
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:93736 Phosphorylation of 9-(2-phosphonomethoxyethyl)adenine and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine by AMP(dAMP) kinase from L1210 cells. Merta, Ales; Votruba, Ivan; Jindrich, Jindrich; Holy, Antonin; Cihlar, Tomas; Rosenberg, Ivan; Otmar, Miroslav; Herve, Tchaou Y. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Biochem. Pharmacol., 44(10), 2067-77 (English) 1992. CODEN: BCPCA6. ISSN: 0006-2952.

AB The acyclic nucleotide analogs 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), which display potent antiviral activity, are transformed in the cells to their mono- and diphosphoryl derivs. The enzyme that in 2 steps phosphorylates PMEA and HPMPA to their diphosphoryl derivs. was purified from mouse L1210 cells. The enzyme co-purified with AMP (dAMP) kinase activity; the best substrates of this enzyme were AMP, ADP, and dAMP. Other nucleoside 5'-triphosphates or creatine phosphate could not be substituted for ATP as a phosphate donor. At least one other enzyme (creatine kinase) can transform the monophosphoryl derivs. of the studied compds. to their resp. diphosphates.

L13 ANSWER 67 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 145899-92-9 REGISTRY
CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)-1-(hydroxymethyl)ethoxy]methyl]phosphonic acid, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C9 H16 N5 O11 P3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:93736 Phosphorylation of 9-(2-phosphonomethoxyethyl)adenine and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine by AMP(dAMP) kinase from L1210 cells. Merta, Ales; Votruba, Ivan; Jindrich, Jindrich; Holy, Antonin; Cihlar, Tomas; Rosenberg, Ivan; Otmar, Miroslav; Herve, Tchaou Y. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Biochem. Pharmacol., 44(10), 2067-77 (English) 1992. CODEN: BCPCA6. ISSN: 0006-2952.

AB The acyclic nucleotide analogs 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), which display potent antiviral activity, are transformed in the cells to their mono- and diphosphoryl derivs. The enzyme that in 2 steps phosphorylates PMEA and HPMPA to their diphosphoryl derivs. was purified from mouse L1210 cells. The enzyme co-purified with AMP (dAMP) kinase activity; the best substrates of this enzyme were AMP, ADP, and dAMP. Other nucleoside 5'-triphosphates or creatine phosphate could not be substituted for ATP as a phosphate donor. At least one other enzyme (creatine kinase) can transform the monophosphoryl derivs. of the studied compds. to their resp. diphosphates.

L13 ANSWER 68 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 145899-77-0 REGISTRY

CN Isohypophosphoric acid, [[2-(6-amino-9H-purin-9-yl)-1-(hydroxymethyl)ethoxy]methyl]-, (R)- (9CI) (CA INDEX NAME)

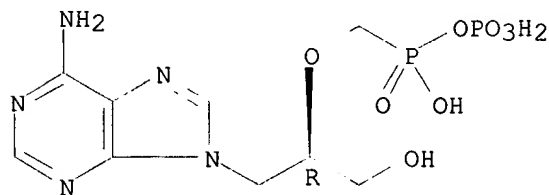
FS STEREOSEARCH

MF C9 H15 N5 O8 P2

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:93736 Phosphorylation of 9-(2-phosphonomethoxyethyl)adenine

Searched by: Mary Hale 308-4258 CM-1 12D16

and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine by AMP(dAMP) kinase from L1210 cells. Merta, Ales; Votruba, Ivan; Jindrich, Jindrich; Holy, Antonin; Cihlar, Tomas; Rosenberg, Ivan; Otmar, Miroslav; Herve, Tchaou Y. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Biochem. Pharmacol., 44(10), 2067-77 (English) 1992. CODEN: BCPCA6. ISSN: 0006-2952.

AB The acyclic nucleotide analogs 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), which display potent antiviral activity, are transformed in the cells to their mono- and diphosphoryl derivs. The enzyme that in 2 steps phosphorylates PMEA and HPMPA to their diphosphoryl derivs. was purified from mouse L1210 cells. The enzyme co-purified with AMP (dAMP) kinase activity; the best substrates of this enzyme were AMP, ADP, and dAMP. Other nucleoside 5'-triphosphates or creatine phosphate could not be substituted for ATP as a phosphate donor. At least one other enzyme (creatine kinase) can transform the monophosphoryl derivs. of the studied compds. to their resp. diphosphates.

L13 ANSWER 69 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 139211-49-7 REGISTRY

CN Phosphonic acid, [[[[2-[(6-amino-9H-purin-9-yl)oxy]ethoxy)methyl]hydroxyphosphinyl)methyl]- (9CI) (CA INDEX NAME)

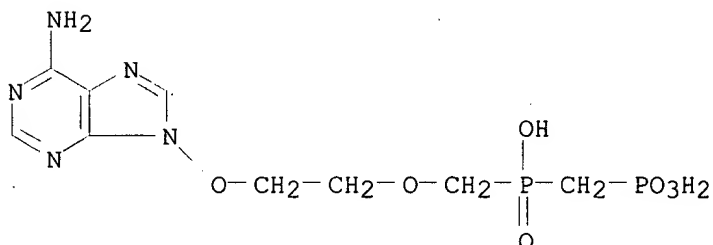
FS 3D CONCORD

MF C9 H15 N5 O7 P2

SR CA

LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:106686 Analogs of acyclonucleoside diphosphates. The synthesis of a series of diphosphonate derivatives of pyrimidines and purines. Parkin, Ann (SmithKline Beecham Pharm., Epsom/Surrey, KT18 5XQ, UK). J. Chem. Soc., Perkin Trans. 1 (12), 2983-90 (English) 1991. CODEN: JCPRB4. ISSN: 0300-922X.

AB (HO)2P(O)CH2P(O)(OH)CH2CH2OR1 (I; R = H, CH2OH; R1 = uracil, thymine, cytosine, guanine, adenine) were prepd. The diphosphonate unit was introduced into suitably functionalized alcs. by use of (EtO)2P(O)CH2P(O)(OEt)2. Mitsunobu coupling of (EtO)2P(O)CH2P(O)(OEt)CH2CH2R2 CH2OH (R2 = H, CH2OAc) with 1-hydroxypyrimidines and 9-hydroxypurines provided a general route to the protected derivs. of I. Conventional deprotection techniques afforded I. Some I have antiviral activity.

L13 ANSWER 70 OF 166 REGISTRY COPYRIGHT 2002 ACS

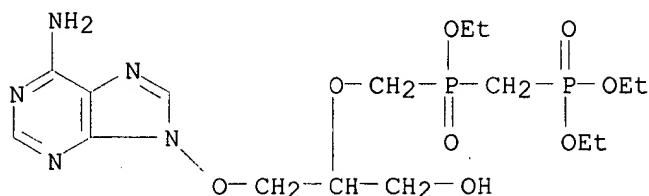
RN 139211-48-6 REGISTRY

CN Phosphonic acid, [[[[2-[(6-amino-9H-purin-9-yl)oxy]-1-

Searched by: Mary Hale 308-4258 CM-1 12D16

(hydroxymethyl)ethoxy)methyl]ethoxyphosphinyl)methyl]-, diethyl ester,
monohydrochloride (9CI) (CA INDEX NAME)

MF C16 H29 N5 O8 P2 . Cl H
SR CA
LC STN Files: CA, CAPLUS



● HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:106686 Analogs of acyclonucleoside diphosphates. The synthesis of a series of diphosphonate derivatives of pyrimidines and purines. Parkin, Ann (SmithKline Beecham Pharm., Epsom/Surrey, KT18 5XQ, UK). J. Chem. Soc., Perkin Trans. 1 (12), 2983-90 (English) 1991. CODEN: JCPRB4. ISSN: 0300-922X.

AB (HO)2P(O)CH2P(O)(OH)CHRCH2OR1 (I; R = H, CH2OH; R1 = uracil, thymine, cytosine, guanine, adenine) were prepd. The diphosphonate unit was introduced into suitably functionalized alcs. by use of (EtO)2P(O)CH2P(OEt)2. Mitsunobu coupling of (EtO)2P(O)CH2P(O)(OEt)CH2CHR2CH2OH (R2 = H, CH2OAc) with 1-hydroxypyrimidines and 9-hydroxypurines provided a general route to the protected derivs. of I. Conventional deprotection techniques afforded I. Some I have antiviral activity.

L13 ANSWER 71 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 139211-47-5 REGISTRY

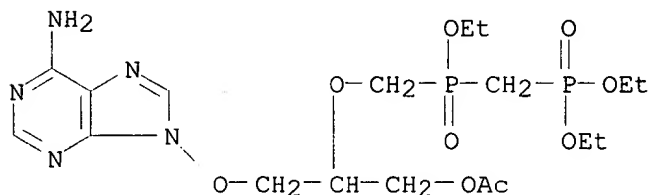
CN Phosphonic acid, [[[[[2-(acetyloxy)-1-[[[(6-amino-9H-purin-9-yl)oxy)methyl]ethoxy)methyl]ethoxyphosphinyl)methyl]-, diethyl ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C18 H31 N5 O9 P2

SR CA

LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

REFERENCE 1: 116:106686 Analogs of acyclonucleoside diphosphates. The synthesis of a series of diphosphonate derivatives of pyrimidines and purines. Parkin, Ann (SmithKline Beecham Pharm., Epsom/Surrey, KT18 5XQ, UK). J. Chem. Soc., Perkin Trans. 1 (12), 2983-90 (English) 1991. CODEN: JCPRB4. ISSN: 0300-922X.

AB (HO)2P(O)CH2P(O)(OH)CHRCH2OR1 (I; R = H, CH2OH; R1 = uracil, thymine, cytosine, guanine, adenine) were prepd. The diphosphonate unit was introduced into suitably functionalized alcs. by use of (EtO)2P(O)CH2P(OEt)2. Mitsunobu coupling of (EtO)2P(O)CH2P(O)(OEt)CH2CHR2CH2OH (R2 = H, CH2OAc) with 1-hydroxypyrimidines and 9-hydroxypurines provided a general route to the protected derivs. of I. Conventional deprotection techniques afforded I. Some I have antiviral activity.

L13 ANSWER 72 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 139211-46-4 REGISTRY

CN Phosphonic acid, [[[[2-[(6-amino-9H-purin-9-yl)oxy]ethoxy]methyl]ethoxyphosphinyl]methyl]-, diethyl ester (9CI) (CA INDEX NAME)

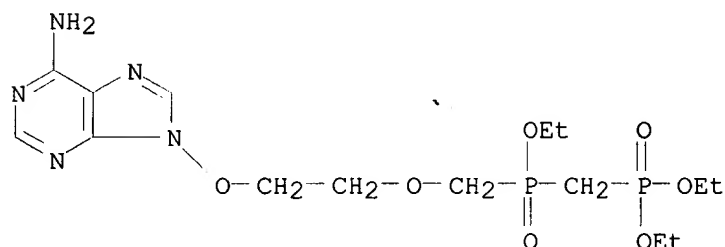
FS 3D CONCORD

MF C15 H27 N5 O7 P2

SR CA

LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:106686 Analogs of acyclonucleoside diphosphates. The synthesis of a series of diphosphonate derivatives of pyrimidines and purines. Parkin, Ann (SmithKline Beecham Pharm., Epsom/Surrey, KT18 5XQ, UK). J. Chem. Soc., Perkin Trans. 1 (12), 2983-90 (English) 1991. CODEN: JCPRB4. ISSN: 0300-922X.

AB (HO)2P(O)CH2P(O)(OH)CHRCH2OR1 (I; R = H, CH2OH; R1 = uracil, thymine, cytosine, guanine, adenine) were prepd. The diphosphonate unit was introduced into suitably functionalized alcs. by use of (EtO)2P(O)CH2P(OEt)2. Mitsunobu coupling of (EtO)2P(O)CH2P(O)(OEt)CH2CHR2CH2OH (R2 = H, CH2OAc) with 1-hydroxypyrimidines and 9-hydroxypurines provided a general route to the protected derivs. of I. Conventional deprotection techniques afforded I. Some I have antiviral activity.

L13 ANSWER 73 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 139177-59-6 REGISTRY

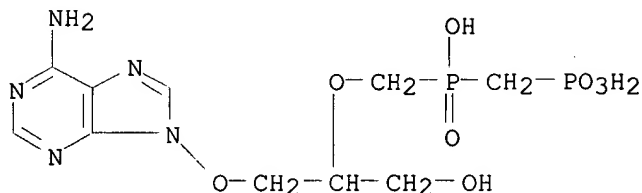
CN Phosphonic acid, [[[[2-[(6-amino-9H-purin-9-yl)oxy]-1-(hydroxymethyl)ethoxy]methyl]hydroxyphosphinyl]methyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phosphonic acid, [[[[2-[(6-amino-9H-purin-9-yl)oxy]-1-

Searched by: Mary Hale 308-4258 CM-1 12D16

(hydroxymethyl)ethoxy)methyl]hydroxyphosphinyl)methyl]-, (.+-.)-
 FS 3D CONCORD
 MF C10 H17 N5 O8 P2
 SR CA
 LC STN Files: BEILSTEIN*, CA, CAPLUS
 (*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:106686 Analogs of acyclonucleoside diphosphates. The synthesis of a series of diphosphonate derivatives of pyrimidines and purines. Parkin, Ann (SmithKline Beecham Pharm., Epsom/Surrey, KT18 5XQ, UK). J. Chem. Soc., Perkin Trans. 1 (12), 2983-90 (English) 1991. CODEN: JCPRB4. ISSN: 0300-922X.

AB (HO)2P(O)CH2P(O)(OH)CHRCH2OR1 (I; R = H, CH2OH; R1 = uracil, thymine, cytosine, guanine, adenine) were prepd. The diphosphonate unit was introduced into suitably functionalized alcs. by use of (EtO)2P(O)CH2P(OEt)2. Mitsunobu coupling of (EtO)2P(O)CH2P(O)(OEt)CH2CHR2CH2OH (R2 = H, CH2OAc) with 1-hydroxypyrimidines and 9-hydroxypurines provided a general route to the protected derivs. of I. Conventional deprotection techniques afforded I. Some I have antiviral activity.

L13 ANSWER 74 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 135484-49-0 REGISTRY

CN Isophosphoric acid, [[2-(6-amino-9H-purin-9-yl)-1-(fluoromethyl)ethoxy)methyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

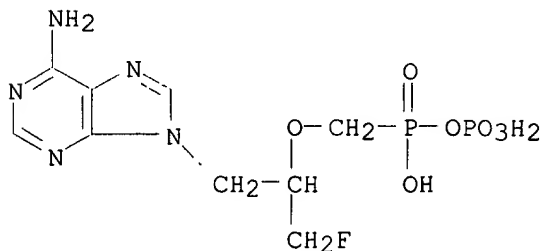
CN Isophosphoric acid, [[2-(6-amino-9H-purin-9-yl)-1-(fluoromethyl)ethoxy)methyl]-, (.+-.)-

FS 3D CONCORD

MF C9 H14 F N5 O7 P2

SR CA

LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

Searched by: Mary Hale 308-4258 CM-1 12D16

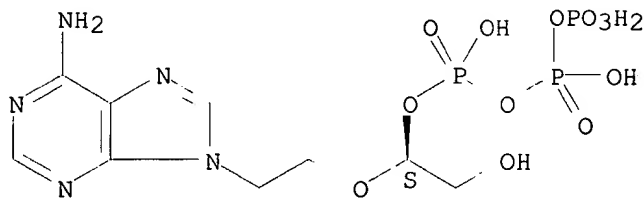
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:174107 9-[(2RS)-3-Fluoro-2-phosphonylmethoxypropyl]
derivatives of purines: a class of highly selective antiretroviral agents
in vitro and in vivo. Balzarini, Jan; Holy, A.; Jindrich, J.; Dvorakova,
H.; Hao, Z.; Snoeck, R.; Herdewijn, P.; Johns, D. G.; De Clercq, Erik
(Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.).
Proc. Natl. Acad. Sci. U. S. A., 88(11), 4961-5 (English) 1991. CODEN:
PNASA6. ISSN: 0027-8424.

AB A new class of compds., 9-[(2RS)-3-fluoro-2-phosphonylmethoxypropyl]
[(RS)-FPMP] derivs. of purines, is described that has selective activity
against a broad spectrum of retroviruses [including human immunodeficiency
virus type 1 (HIV-1) and type 2 (HIV-2)] but not other RNA or DNA viruses.
This activity spectrum is completely different from that of the parental
compds., 9-[(2S)-3-hydroxy-2-phosphonylmethoxypropyl] [(S)-HPMP] derivs.
of purines, which are active against a broad range of DNA viruses. The
racemic (RS)-FPMP derivs. of adenine and 2,6-diaminopurine, termed
(RS)-FPMPA and (RS)-FPMPDAP, resp., are markedly more selective as in
vitro antiretroviral agents than their 9-(2-phosphonylmethoxyethyl) (PME)
counterparts, PMEA and PMEDAP. Also, (RS)-FPMPA and (RS)-FPMPDAP have a
substantially higher therapeutic index in mice in inhibiting Moloney
murine sarcoma virus-induced tumor formation and assocd. death and are
markedly less inhibitory to human bone marrow cells than PEMA and PMEDAP.
The diphosphate deriv. of (RS)-FPMPA [(RS)-FPMPApp] is a potent and
selective inhibitor of HIV-1 reverse transcriptase but not of HSV-1 DNA
polymerase or DNA polymerase .alpha.. (RS)-FPMPApp, akin to PMEA
diphosphate (PMEApp), acts as a DNA chain terminator. The DNA
chain-terminating properties of PMEApp and (RS)-FPMPApp seem to be a
prerequisite for acyclic nucleoside phosphonates to exhibit antiretrovirus
(i.e., anti-HIV) activity.

L13 ANSWER 75 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 130622-58-1 REGISTRY
CN Triphosphoric acid, P-[1-[2-(6-amino-9H-purin-9-yl)ethoxy]-2-hydroxyethyl]
ester, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C9 H16 N5 O12 P3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 113:224152 Inhibition of herpes simplex virus DNA polymerase by
diphosphates of acyclic phosphonylmethoxyalkyl nucleotide analogs. Merta,
Ales; Votruba, Ivan; Rosenberg, Ivan; Otmar, Miroslav; Hrebabecky, Hubert;

Searched by: Mary Hale 308-4258 CM-1 12D16

Holy, Antonin (Inst. Org. Chem. Biochem., Slovak Acad. Sci., Prague, 16610/6, Czech.). Antiviral Res., 13(5), 209-18 (English) 1990. CODEN: ARSRDR. ISSN: 0166-3542.

AB The inhibition of HSV-1 DNA polymerase and HeLa DNA polymerases .alpha. and .beta. by diphosphoryl derivs. of acyclic phosphonylmethoxyalkyl nucleotide analogs was studied and compared with the inhibition by ACV-TP, araCTP, ddTTP, and AZT-TP. In the series of phosphonylmethoxyethyl (PME-) derivs. of heterocyclic bases, the inhibitory effect of their diphosphates on HSV-1 DNA polymerase decreased in the order 2-amino-PMEApp (Ki = 0.03 .mu.M) .mchgt. PMEGpp > PMEApp > PMETpp .mchgt. PMECpp .mchgt. n8z7PMEApp > PMEUp. The diphosphate deriv. of the antiherpes agent (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA) proved to be a relatively weak inhibitor of HSV-1 DNA polymerase (Ki = 1.4 .mu.M). The inhibitors could be divided into three groups: (a) the diphosphoryl derivs. of acyclic nucleotide analogs (PME-type and HPMPA) and ACV-TP specifically inhibit HSV-1 DNA polymerase and DNA polymerase .alpha. and do not inhibit DNA polymerase .beta.; (b) AZT-TP and ddTTP are effective only against DNA polymerase .beta., and (c) araCTP inhibits all three enzymes. When dATP was omitted from the reaction mixt., the addn. of HPMPApp stimulated DNA synthesis by HSV-1 DNA polymerase indicating that HPMPApp is an alternative substrate for in vitro DNA synthesis catalyzed by this enzyme.

L13 ANSWER 76 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 130029-10-6 REGISTRY

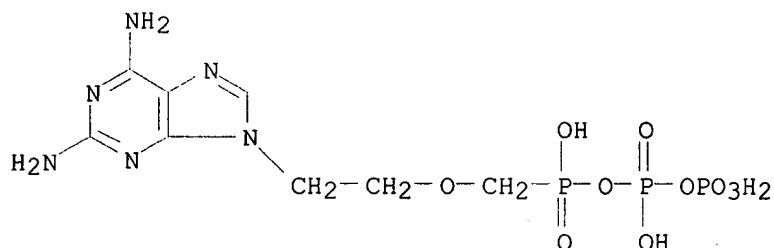
CN Diphosphoric acid, monoanhydride with [[2-(2,6-diamino-9H-purin-9-yl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C8 H15 N6 O10 P3

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

6 REFERENCES IN FILE CA (1967 TO DATE)

6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:58689 9-(2-Phosphonylmethoxyethyl) derivatives of purine nucleotide analogs: A comparison of their metabolism and interaction with cellular DNA synthesis. Kramata, Pavel; Downey, Kathleen M. (Gilead Sciences, Foster City, CA, USA). Molecular Pharmacology, 56(6), 1262-1270 (English) 1999. CODEN: MOPMA3. ISSN: 0026-895X. Publisher: American Society for Pharmacology and Experimental Therapeutics.

AB Incubation of CEM cells for 24 h with the guanine, 2,6-diaminopurine, and adenine nucleotide analogs of the 9-(2-phosphonylmethoxyethyl) series, 9-(2-phosphonylmethoxyethyl)guanine (PMEG), 9-(2-phosphonylmethoxyethyl)-2,6-diaminopurine (PMEDAP), and 9-(2-phosphonylmethoxyethyl)adenine (PMEA), was found to inhibit DNA synthesis 50% at concns. of 1, 6, and 25 .mu.M, resp. Possible reasons for the marked differences were

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investigated, including cellular transport of the analogs, different efficiencies of intracellular phosphorylation, differential effects on 2'-deoxynucleotide (dNTP) pools, and differences in the affinities of the cellular DNA polymerases for the diphosphate derivs. of the drugs. No significant differences in cellular uptake were found among the analogs; however, they did differ in the efficiency of phosphorylation, i.e., CEM cells were found to accumulate higher levels of PMEG-diphosphate (PMEGpp) than PMEDAP-diphosphate (PMEDAPpp) or PMEA-diphosphate (PMEApp). Treatment of cells with any of the nucleotide analogs resulted in increased dNTP pools, with PMEG producing the greatest increase. All three analogs had the greatest effect on the dATP pool size, whereas the dGTP pool size was not significantly affected. Comparison of the ratios of nucleotide analog diphosphates to their corresponding dNTPs under conditions where DNA synthesis is inhibited 50% suggested that cellular DNA polymerases were approx. twice as sensitive to PMEGpp than to PMEDAPpp and 5-fold more sensitive to PMEGpp than to PMEApp. Consistent with this hypothesis, examn. of the efficiencies with which the replicative DNA polymerases .alpha., .delta., and .epsilon. incorporated the analogs showed that DNA polymerase .delta., the most sensitive of the DNA polymerases, incorporated PMEGpp twice as efficiently as PMEDAPpp and 7-fold more efficiently than PMEApp.

REFERENCE 2: 125:268990 Structural features of acyclic nucleotide analogs conferring inhibitory effects on cellular replicative DNA polymerases. Kramata, Pavel; Birkus, Gabriel; Otmar, Miroslav; Votruba, Ivan; Holy, Antonin (Institute Organic Chemistry Biochemistry, Academy Sciences Czech Republic, Prague, 166 10, Czech Rep.). Collect. Czech. Chem. Commun., 61(Spec. Issue), S188-S191 (English) 1996. CODEN: CCCCAK. ISSN: 0010-0765.

AB Diphosphates of phosphonomethoxyalkyl acyclic nucleotide analogs were tested as inhibitors of two proteolyzed forms of cellular repetitive DNA polymerase .epsilon., and DNA polymerases .alpha. and .delta.. The Ki/Km ratios are given. Effects of different substitutions on their inhibitory activity are discussed.

REFERENCE 3: 125:104413 Different inhibitory potencies of acyclic phosphonomethoxyalkyl nucleotide analogs toward DNA polymerases .alpha., .delta., and .epsilon.. Kramata, Pavel; Votruba, Ivan; Otova, Berta; Holy, Antonin (Inst. of Organic Chemistry and Biochemistry, Acad. of Sci. of The Czech Republic, Prague, 16610, Czech Rep.). Mol. Pharmacol., 49(6), 1005-1011 (English) 1996. CODEN: MOPMA3. ISSN: 0026-895X.

AB Based on the powerful virustatic potency and cytostatic activity of adenine, 2,6-diaminopurine, and guanine derivs. of acyclic phosphonate nucleotide analog (S)-1-(3-hydroxy-2-phosphonomethoxypropyl) and 9-(2-phosphonomethoxyethyl) series, we examd. the inhibitory potencies of their diphosphates [(S)-9-(3-hydroxy-2-phosphonomethoxypropyl)adenine diphosphate (HPMPApp), 9-(2-phosphonomethoxyethyl)adenine diphosphate, 9-(2-phosphonomethoxyethyl)-2,6-diaminopurine diphosphate (PMEDAPpp), and 9-(2-phosphonomethoxyethyl)guanine diphosphate, analogs of nucleoside 5'-triphosphate] toward cellular DNA polymerases .alpha., .delta., and .epsilon. (isolated from tumors of T cell spontaneous acute lymphoblastic leukemia in Sprague-Dawley inbred rats). Kinetic measurements (Km, Ki, and Vmax) of synthetic homopolymeric template primers have shown that HPMPApp is a selective and potent inhibitor of polymerase .epsilon., whereas PMEDAPpp strongly inhibits polymerase .delta.. These two compds. may be useful for elucidating the roles of polymerases .delta. and .epsilon.. Of the nucleotide analogs tested, 9-(2-phosphonomethoxyethyl)guanine diphosphate is the most efficient inhibitor of polymerases .alpha. and .epsilon., whereas the diphosphate of 9-(2-phosphonomethoxyethyl)adenine, the therapeutically important agent adefovir, inhibits polymerases .alpha. and .epsilon. relatively poorly and exerts only moderate inhibition of polymerase .delta.. These data are

quite consistent with previously reported cytostatic activity of these nucleotide analogs. All of the enzymes studied catalyze the incorporation of 9-(2-phosphonomethoxyethyl)adenine, 9-(2-phosphonomethoxyethyl)-2,6,-diaminopurine, and (S)-9-3-hydroxy-2-(phosphonomethoxypropyl)adenine into DNA chain. 9-(2-Phosphonomethoxyethyl)adenine diphosphate and HPMPApp were confirmed to be DNA chain terminators. HPMPApp formed poly(dT)/oligo(dA18)-[(S)-9-(3-hydroxy-2-phosphonomethoxypropyl)adenine]₂₋₄ structures.

REFERENCE 4: 114:35417 Inhibition of avian myeloblastosis virus reverse transcriptase by diphosphates of acyclic phosphonylmethyl nucleotide analogs. Votruba, Ivan; Travnicek, Miloslav; Rosenberg, Ivan; Otmar, Miroslav; Merta, Ales; Hrebabecky, Hubert; Holy, Antonin (Inst. Org. Chem. Biochem., Czech Acad. Sci., Prague, 16610, Czech.). Antiviral Res., 13(6), 287-93 (English) 1990. CODEN: ARSRDR. ISSN: 0166-3542.

AB Diphosphates of N-(2-phosphonylmethoxyethyl) derivs. of heterocyclic nucleotide bases were studied in the endogenous oligo(dT)₁₂₋₁₈ primed reaction of reverse transcriptase obtained from detergent-disrupted avian myeloblastosis virus retrovirions. These diphosphates (analogues of nucleotide 5'-triphosphates) exhibited an inhibitory activity towards reverse transcriptase. This inhibitory activity was dependent on the character of the heterocyclic base and decreased in the order: 2-aminoadenine > adenine > guanine >> cytosine >> thymine > uracil. The 2-aminoadenine deriv. was more potent than either AZT-TP or ddTTP, while phosphonylmethoxyethyladenine had approx. the same potency as the two ref. compds. (IC₅₀ approx. 1 .mu.M AT 20 .mu.M competing substrate). This finding is consistent with the antiviral activity of the parent nucleotide analogs against retroviruses (including HIV).

REFERENCE 5: 113:224152 Inhibition of herpes simplex virus DNA polymerase by diphosphates of acyclic phosphonylmethoxyalkyl nucleotide analogs. Merta, Ales; Votruba, Ivan; Rosenberg, Ivan; Otmar, Miroslav; Hrebabecky, Hubert; Holy, Antonin (Inst. Org. Chem. Biochem., Slovak Acad. Sci., Prague, 16610/6, Czech.). Antiviral Res., 13(5), 209-18 (English) 1990. CODEN: ARSRDR. ISSN: 0166-3542.

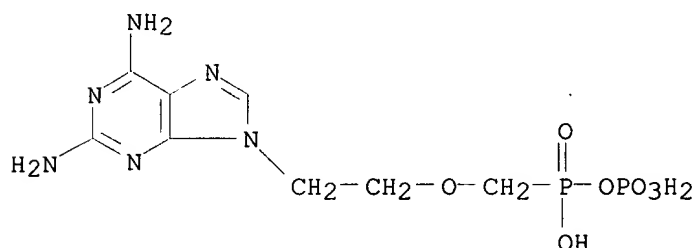
AB The inhibition of HSV-1 DNA polymerase and HeLa DNA polymerases .alpha. and .beta. by diphosphoryl derivs. of acyclic phosphonylmethoxyalkyl nucleotide analogs was studied and compared with the inhibition by ACV-TP, araCTP, ddTTP, and AZT-TP. In the series of phosphonylmethoxyethyl (PME-) derivs. of heterocyclic bases, the inhibitory effect of their diphosphates on HSV-1 DNA polymerase decreased in the order 2-amino-PMEApp (K_i = 0.03 .mu.M) .mchgt. PMEGpp > PMEApp > PMETpp .mchgt. PMECpp .mchgt. n8z7PMEApp > PMEUp. The diphosphate deriv. of the antiherpes agent (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA) proved to be a relatively weak inhibitor of HSV-1 DNA polymerase (K_i = 1.4 .mu.M). The inhibitors could be divided into three groups: (a) the diphosphoryl derivs. of acyclic nucleotide analogs (PME-type and HPMPA) and ACV-TP specifically inhibit HSV-1 DNA polymerase and DNA polymerase .alpha. and do not inhibit DNA polymerase .beta.; (b) AZT-TP and ddTTP are effective only against DNA polymerase .beta., and (c) araCTP inhibits all three enzymes. When dATP was omitted from the reaction mixt., the addn. of HPMPApp stimulated DNA synthesis by HSV-1 DNA polymerase indicating that HPMPApp is an alternative substrate for in vitro DNA synthesis catalyzed by this enzyme.

REFERENCE 6: 113:184251 Phosphonylmethyl ethers of acyclic nucleoside analogs: inhibitors of HSV-1 induced ribonucleotide reductase. Cerny, Jaroslav; Votruba, Ivan; Vonka, Vladimir; Rosenberg, Ivan; Otmar, Miroslav; Holy, Antonin (Inst. Org. Chem. Biochem., Slovak Acad. Sci., Prague, 16610/6, Czech.). Antiviral Res., 13(5), 253-63 (English) 1990. CODEN: ARSRDR. ISSN: 0166-3542.

AB Diphosphates of N-(S)-(3-hydroxy-2-phosphonylmethoxypropyl) (HPMP) and

N-(2-phosphonylmethoxyethyl) (PME) derivs. of purine and pyrimidine heterocyclic bases inhibit HSV-1 encoded ribonucleotide reductase. Of the compds. studied, the most efficient inhibitors of CDP redn. (at 5.1 .mu.mol/L) by the HSV-1-encoded enzyme are HPMPApp (IC50 = 0.9 .mu.mol/L) and PMEApp (IC50 = 8 .mu.mol/L). PMEApp does not inhibit the enzyme isolated from the mutant HSV-1 KOS strain which is resistant to PME at a concn. of 100 .mu.g/mL. The enzyme isolated from the PME-resistant virus strain is also sensitive to inhibitory effects of hydroxyurea and HPMPApp. Thus, the inhibitory potency of HPMPApp and PMEApp toward HSV-1 encoded ribonucleotide reductase might be connected with the anti-HSV activity of HPMPA and PME.

L13 ANSWER 77 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 130029-09-3 REGISTRY
 CN Isohypophosphoric acid, [[2-(2,6-diamino-9H-purin-9-yl)ethoxy)methyl]-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C8 H14 N6 O7 P2
 SR CA
 LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

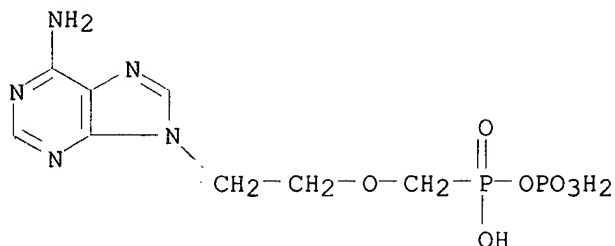
REFERENCE 1: 113:184251 Phosphonylmethyl ethers of acyclic nucleoside analogs: inhibitors of HSV-1 induced ribonucleotide reductase. Cerny, Jaroslav; Votruba, Ivan; Vonka, Vladimir; Rosenberg, Ivan; Otmar, Miroslav; Holy, Antonin (Inst. Org. Chem. Biochem., Slovak Acad. Sci., Prague, 16610/6, Czech.). Antiviral Res., 13(5), 253-63 (English) 1990. CODEN: ARSRDR. ISSN: 0166-3542.

AB Diphosphates of N-(S)-(3-hydroxy-2-phosphonylmethoxypropyl) (HPMP) and N-(2-phosphonylmethoxyethyl) (PME) derivs. of purine and pyrimidine heterocyclic bases inhibit HSV-1 encoded ribonucleotide reductase. Of the compds. studied, the most efficient inhibitors of CDP redn. (at 5.1 .mu.mol/L) by the HSV-1-encoded enzyme are HPMPApp (IC50 = 0.9 .mu.mol/L) and PMEApp (IC50 = 8 .mu.mol/L). PMEApp does not inhibit the enzyme isolated from the mutant HSV-1 KOS strain which is resistant to PME at a concn. of 100 .mu.g/mL. The enzyme isolated from the PME-resistant virus strain is also sensitive to inhibitory effects of hydroxyurea and HPMPApp. Thus, the inhibitory potency of HPMPApp and PMEApp toward HSV-1 encoded ribonucleotide reductase might be connected with the anti-HSV activity of HPMPA and PME.

L13 ANSWER 78 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 129556-87-2 REGISTRY
 CN Isohypophosphoric acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]- (9CI)
 (CA INDEX NAME)

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FS 3D CONCORD
 MF C8 H13 N5 O7 P2
 CI COM
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1967 TO DATE)
 13 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:219407 In vitro evaluation of hepatitis B virus polymerase mutations associated with famciclovir resistance. Xiong, Xiaofeng; Yang, Huiling; Westland, Christopher E.; Zou, Ruiming; Gibbs, Craig S. (Gilead Sciences, Foster City, CA, 94404, USA). Hepatology (Philadelphia), 31(1), 219-224 (English) 2000. CODEN: HPTLD9. ISSN: 0270-9139. Publisher: W. B. Saunders Co..

AB Several mutations (V521L, P525L, L528M, T532S, and V555I) in the gene for hepatitis B virus (HBV) polymerase have been identified in HBV isolated from patients that displayed break-through viremia during famciclovir treatment. To det. whether these mutations cause phenotypic resistance to famciclovir, the authors compared the inhibition consts. (Ki) of penciclovir triphosphate (PCVTP, the active metabolite of famciclovir) for recombinant wild-type and mutant HBV polymerases contg. these mutations. In in vitro enzymic assays, the V555I mutation displayed the most resistance (with Ki increased by 6.2-fold) to PCVTP. The V521L and L528M mutations showed moderately decreased sensitivity to PCVTP (Ki increased by > 3-fold). The authors also analyzed the cross-resistance profiles of these variants for adefovir and lamivudine, two other antiviral agents that also inhibit DNA replication by HBV polymerase. All 5 famciclovir-assocd. mutations were sensitive to adefovir diphosphate (ADVDP) in in vitro enzymic assays (<2.3-fold decreased sensitivity). The V521L, L528M, and T532S mutations were also sensitive to lamivudine triphosphate (LAMTP); however, the P525L and V555I mutations displayed moderately decreased sensitivity to LAMTP in enzymic assays (3.6-fold decreased sensitivity). The lamivudine-resistant mutations M552I, M552V, and L528M+M552V, which were previously shown to display 8- to 25-fold resistance to LAMTP, were less resistant (.ltoreq. 3.1-fold) to PCVTP.

REFERENCE 2: 130:217639 Mutations in hepatitis B DNA polymerase associated with resistance to lamivudine do not confer resistance to adefovir in vitro. Xiong, Xiaofeng; Flores, Carmina; Yang, Huiling; Toole, John J.; Gibbs, Graig S. (Gilead Sciences, Foster City, CA, 94404, USA). Hepatology (Philadelphia), 28(6), 1669-1673 (English) 1998. CODEN: HPTLD9. ISSN: 0270-9139. Publisher: W. B. Saunders Co..

AB To det. whether adefovir is active against lamivudine-resistant hepatitis B virus (HBV), the inhibition consts. of adefovir diphosphate and lamivudine triphosphate for wild-type and mutant human HBV DNA polymerases, which contain amino acid substitutions assocd. with

lamivudine resistance, were compared. Recombinant wild-type and mutant human HBV DNA polymerases were expressed and substantially purified using a baculovirus expression system and immunoaffinity chromatog. HBV DNA polymerase mutants M552I, M552V, and L528M/M552V showed resistance to lamivudine triphosphate with inhibition consts. (K_i) increased by 8.0-fold, 19.6-fold, and 25.2-fold compared with that of wild-type HBV DNA polymerase. However, these mutants remained sensitive to adefovir diphosphate with the inhibition consts. increasing by 1.3-fold and 2.2-fold or decreasing by 0.79-fold. The L528M single mutation, identified in patients with increasing HBV DNA levels during therapy with famciclovir, also remained sensitive to adefovir diphosphate with the inhibition const. increased by only 2.3-fold.

REFERENCE 3: 127:144785 (S)-1-(3-Hydroxy-2-phosphonylmethoxypropyl)cytosine (HPMPC) inhibits HIV-1 replication in epithelial cells, but not T-lymphocytes. Srinivas, Ranga V.; Connely, Michele; Fridland, Arnold (Dep. Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA). Antiviral Research, 35(1), 23-27 (English) 1997. CODEN: ARSRDR. ISSN: 0166-3542. Publisher: Elsevier.

AB PMEA [9-(2-phosphonylmethoxyethyl)adenine] inhibited both HSV-1 and HIV-1 replication in MT-2 and HeLa-CD4 cells. (S)-1-[3-hydroxy-2-(phosphonylmethoxy)propyl]cytosine (HPMPC) inhibited both these viruses in the epithelioid HeLa-CD4 cells, but did not inhibit either virus in the T-lymphocytic MT-2 cells. PMEA and HPMPC are metabolized to their diphosphorylated forms within cells, which then inhibit viral polymerases. We therefore compared the metab. of PMEA and HPMPC in MT-2 and HeLa-CD4 cells. PMEA formation was efficient in both the cell types, whereas HPMPC levels were .apprx.3-10 fold lower in MT-2 cells, compared to HeLa-CD4 cells. These results indicate that HPMPC can inhibit HIV replications in the appropriate cell types, and show that differences in their metab. cannot account entirely for the lack of antiviral efficacy of HPMPC in MT-2 cells.

REFERENCE 4: 123:305901 Metabolic pathways for activation of the antiviral agent 9-(2-phosphonylmethoxyethyl)adenine in human lymphoid cells. Robbins, Brian L.; Greenhaw, Jack; Connolly, Michelle C.; Fridland, Arnold (Dep. Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA). Antimicrob. Agents Chemother., 39(10), 2304-8 (English) 1995. CODEN: AMACQ. ISSN: 0066-4804.

AB 9-(2-Phosphonylmethoxyethyl)adenine (PMEA), the acyclic phosphonate analog of adenine monophosphate, is a promising antiviral drug with activity against herpesviruses, Epstein-Barr virus, and retroviruses, including the human immunodeficiency virus. To be active, it must be converted to the diphosphate deriv., the putative inhibitor of viral DNA polymerases. The metabolic pathway responsible for activation of PMEA is unclear. The metab. of PMEA was investigated in human T-lymphoid cells (CEMss) and a PMEA-resistant subline (CEMssr-1) with a partial deficiency in adenylate kinase activity. Expts. with [3H]PMEA showed that exts. of CEMss phosphorylated PMEA to its mono- and diphosphate in the presence of ATP as the phosphate donor. No other nucleotides or 5-phosphoribosyl pyrophosphate displayed appreciable activity as a phosphate donor. Subcellular fractionation expts. showed that CEMss cells contained two nucleotide kinase activities, one in mitochondria and one in the cytosol, which phosphorylated PMEA. The PMEA-resistant CEMss mutant proved to have a deficiency in the mitochondrial adenylate kinase activity, indicating that this enzyme was important in the phosphorylation of PMEA. Other effective antiviral purine phosphonate derivs. of PMEA showed a profile of phosphorylating activity similar to that of PMEA. By comparison, phosphorylation of the pyrimidine analog (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl)cytosine proceeded by an enzyme present in the cytosol. The authors conclude from these studies that adenylate kinase which has been localized in the intermembrane space of mitochondria is the

major route for PMEAs phosphorylation in CEMss cells but that another hitherto unidentified enzyme(s) present in the cytosol may contribute to the anabolism of the phosphonates.

REFERENCE 5: 122:281663 Metabolic diversity and antiviral activities of acyclic nucleoside phosphonates. Aduma, Philip; Connelly, Michele C.; Srinivas, Ranga V.; Fridland, Arnold (Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA). Mol. Pharmacol., 47(4), 816-22 (English) 1995. CODEN: MOPMA3. ISSN: 0026-895X.

AB The acyclic nucleoside phosphonates (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl)cytosine (HPMPC), (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA), and 9-(2-phosphonylmethoxyethyl)adenine (PMEA) inhibited herpes simplex virus-1 replication in Vero cells, and the IC₅₀ values ranged from 4 μ M (for HPMPC and HPMPA) to 40 μ M (for PMEAs). Pretreatment of cells with HPMPC for 12-24 h induced an effective antiviral state, and the cells maintained this antiviral state for > 7 days. In contrast, much larger amounts (.apprx.2.5-5 .times. IC₅₀ doses) of PMEAs or HPMPA were required to establish an antiviral state, which lasted for only .apprx.24 or 72 h, resp. A 12-h treatment of the cells with the phosphonates was required for the establishment of optimal antiviral activity; surprisingly, longer durations of exposure to PMEAs (but not HPMPA or HPMPC) resulted in diminished antiviral effect. The authors investigated the metab. of PMEAs and HPMPC to det. the cellular basis for these differences. The cellular uptake of HPMPC was .apprx.8-fold greater than that of PMEAs. The levels of the PMEAs metabolites PMEAs monophosphate and PMEAs diphosphate increased for .apprx.12 h and plateaued thereafter. PMEAs and its metabolites were cleared from the cells with a half-life of 4.9 h. In contrast, the HPMPC metabolites HPMPC monophosphate (HPMPCp) and HPMPC diphosphate (HPMPCpp) accumulated throughout the 24-h study period and, at equimolar drug concns. (25 μ M), reached intracellular levels .apprx.2-3-fold greater than those of the PMEAs metabolites. HPMPC also differed from PMEAs in its capacity to generate a phosphodiester metabolite (HPMPCp-choline), which was a predominant metabolite in HPMPC-treated cells. In addn., the rates of disappearance of intracellular metabolites of the two drugs were significantly different. Thus, the decay of HPMPCpp was quite slow and biphasic (t_{1/2} = 24 and 65 h) and that of HPMPCp-choline was monophasic (t_{1/2} = 87 h). Together, these factors can explain the differing antiviral potencies seen with PMEAs and HPMPC. The possible role of the choline adduct in the expression of antiviral activity of the drug remains to be elucidated, but the adduct may serve as an intracellular store for the long term maintenance of active HPMPCpp in cells. The results also highlight the extent of diversity in the cellular pharmacol. and antiviral activities of the acyclic nucleoside phosphonates.

REFERENCE 6: 122:177788 A human T lymphoid cell variant resistant to the acyclic nucleoside phosphonate 9-(2-phosphonylmethoxyethyl)adenine shows a unique combination of a phosphorylation defect and increased efflux of the agent. Robbins, Brian L.; Connelly, Michele C.; Marshall, Dana R.; Srinivas, Ranga V.; Fridland, Arnold (Dep. Infectious Dis., St. Jude Children's Res. Hosp., Memphis, TN, 38105, USA). Mol. Pharmacol., 47(2), 391-7 (English) 1995. CODEN: MOPMA3. ISSN: 0026-895X.

AB 9-(2-Phosphonylmethoxyethyl)adenine (PMEA) is a new antiviral agent with activity against herpes viruses and retroviruses, including human immunodeficiency virus, but its metab. and mechanism of action remain unclear. The authors have isolated a human T lymphoid cell line (CEM-r1) that is resistant to the antiproliferative effects of PMEAs. The antiviral effects of PMEAs against human immunodeficiency virus-1 infection were also greatly reduced in CEM-r1 cells, compared with the parental cells. This mutant showed cross-resistance to the related acyclic nucleoside phosphonates 9-(2-phosphonylmethoxyethyl)diaminopurine and

9-(2-phosphonylmethoxyethyl)guanine and the lipophilic prodrug bis(pivaloyloxymethyl)-9-(2-phosphonylmethoxyethyl)adenine (bispom-PMEA), as well as partial resistance to the purine nucleosides 2-chlorodeoxyadenosine, 2-fluoro-9-.beta.-D-arabinosylfuranosyladenine, and adenosine, but did not show resistance to 2'-deoxyadenosine or 9-.beta.-D-arabinosylfuranosyladenine. The authors compared the uptake and metab. of [3H]PMEA and [3H]bispom-PMEA in the mutant and parental cells. The anal. of radioactive products by high pressure liq. chromatog. revealed marked alterations in the ability of the mutant cell line to accumulate PMEA and its anabolites, compared with the parental cells. Accumulation of PMEA, PMEA monophosphate, and PMEA bisphosphate (major metabolites formed with either PMEA or bispom-PMEA) decreased by 50, 95, and 97%, resp. Compared with the parental cells, the variant cells showed a .apprx.7-fold increase in the rate of efflux of PMEA and a 2-fold decrease in the activity of adenylate kinase. In contrast, other enzymes of nucleotide metab., such as adenosine kinase, deoxycytidine kinase, and 5-phosphoribosyl-1-pyrophosphate synthetase, showed no significant change in the two cell lines. Overall, these results suggest that the mutation in this resistant cell line is of a novel type, involving an alteration in the cellular efflux of PMEA as the major basis for the resistant phenotype.

REFERENCE 7: 118:93736 Phosphorylation of 9-(2-phosphonomethoxyethyl)adenine and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine by AMP(dAMP) kinase from L1210 cells. Merta, Ales; Votruba, Ivan; Jindrich, Jindrich; Holy, Antonin; Cihlar, Tomas; Rosenberg, Ivan; Otmar, Miroslav; Herve, Tchaou Y. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Biochem. Pharmacol., 44(10), 2067-77 (English) 1992. CODEN: BCPA6. ISSN: 0006-2952.

AB The acyclic nucleotide analogs 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), which display potent antiviral activity, are transformed in the cells to their mono- and diphosphoryl derivs. The enzyme that in 2 steps phosphorylates PMEA and HPMPA to their diphosphoryl derivs. was purified from mouse L1210 cells. The enzyme co-purified with AMP (dAMP) kinase activity; the best substrates of this enzyme were AMP, ADP, and dAMP. Other nucleoside 5'-triphosphates or creatine phosphate could not be substituted for ATP as a phosphate donor. At least one other enzyme (creatine kinase) can transform the monophosphoryl derivs. of the studied compds. to their resp. diphosphates.

REFERENCE 8: 117:245058 Inhibition of reverse transcriptase from feline immunodeficiency virus by analogs of 2'-deoxyadenosine 5'-triphosphate. Cronn, Richard C.; Remington, Kathryn Martin; Preston, Bradley D.; North, Thomas W. (Div. Biol. Sci., Univ. Montana, Missoula, MT, 59812, USA). Biochem. Pharmacol., 44(7), 1375-81 (English) 1992. CODEN: BCPA6. ISSN: 0006-2952.

AB The replication of feline immunodeficiency virus (FIV) in cultured cells was inhibited by 2',3'-dideoxyadenosine (ddA) and by 9-(2-phosphonylmethoxyethyl)adenine (PMEA) with IC50 values of 0.98 and 0.95 .mu.M, resp. The effects of the presumed active forms of these inhibitors, ddATP and PMEA diphosphate (PMEApp), upon the FIV reverse transcriptase (RT) were examd. with 2 different template-primer systems. Both of these compds. were potent inhibitors of the FIV RT in reactions with primed .vphi.X-174 DNA, yielding Ki values of 8.8 nM for ddATP and 5.0 nM for PMEApp. However, they were both poor inhibitors of the reaction with poly(rU)-oligo(dA); concns. of ddATP or PMEApp >10 .mu.M were required to inhibit this reaction by 50%. Further anal. of the reaction with poly(rU)-oligo(dA) revealed that even in the absence of inhibitors the primers were extended by <20 nucleotides. In contrast, high-mol.-wt. products were obtained in reactions with .vphi.X-174 DNA. These results suggest that the reaction of FIV RT with poly(rU)-oligo(dA)

is not highly processive. The high degree of termination encountered during this reaction with poly(rU)-oligo(dA) may be responsible for the low inhibitory potential of ddATP and PMEApp.

REFERENCE 9: 117:225687 Pharmacokinetics in mice of the anti-retrovirus agent 9-(2-phosphonylmethoxyethyl)adenine. Naesens, Lieve; Balzarini, Jan; De Clercq, Erik (Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.). Drug Metab. Dispos., 20(5), 747-52 (English) 1992. CODEN: DMDSAI. ISSN: 0090-9556.

AB The pharmacokinetics of 9-(2-phosphonylmethoxyethyl)adenine (PMEA), a potent inhibitor of retrovirus (i.e. human immunodeficiency virus) replication was detd. in mice. Upon i.v. bolus administration of PMEa at 25, 100, or 500 mg/kg, PMEa was rapidly cleared from the plasma in a monoexponential and dose-independent manner (half-life, 7-12.5 min; distribution vol., 0.30-0.36 L/kg; total body clearance, 1.21-2.41 L/h/kg). Irresp. of the initial PMEa dose, 67% of unchanged PMEa was recovered from the urine of mice within 24 h after administration of PMEa. [3H]PMEA, administered as an i.v. bolus injection, mainly accumulated in the kidney, liver, and lungs. Significant amts. of monophosphorylated PMEa were detected in kidney and liver, but not other tissues, at 10, 30, and 60 min after i.v. administration of PMEa. Low but significant levels of PMEa were attained in the brain.

REFERENCE 10: 115:174107 9-[(2RS)-3-Fluoro-2-phosphonylmethoxypropyl] derivatives of purines: a class of highly selective antiretroviral agents in vitro and in vivo. Balzarini, Jan; Holy, A.; Jindrich, J.; Dvorakova, H.; Hao, Z.; Snoeck, R.; Herdewijn, P.; Johns, D. G.; De Clercq, Erik (Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.). Proc. Natl. Acad. Sci. U. S. A., 88(11), 4961-5 (English) 1991. CODEN: PNASA6. ISSN: 0027-8424.

AB A new class of compds., 9-[(2RS)-3-fluoro-2-phosphonylmethoxypropyl] [(RS)-FPMP] derivs. of purines, is described that has selective activity against a broad spectrum of retroviruses [including human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2)] but not other RNA or DNA viruses. This activity spectrum is completely different from that of the parental compds., 9-[(2S)-3-hydroxy-2-phosphonylmethoxypropyl] [(S)-HPMP] derivs. of purines, which are active against a broad range of DNA viruses. The racemic (RS)-FPMP derivs. of adenine and 2,6-diaminopurine, termed (RS)-FPMPA and (RS)-FPMPDAP, resp., are markedly more selective as in vitro antiretroviral agents than their 9-(2-phosphonylmethoxyethyl) (PME) counterparts, PMEa and PMEDAP. Also, (RS)-FPMPA and (RS)-FPMPDAP have a substantially higher therapeutic index in mice in inhibiting Moloney murine sarcoma virus-induced tumor formation and assocd. death and are markedly less inhibitory to human bone marrow cells than PEMA and PMEDAP. The diphosphate deriv. of (RS)-FPMPA [(RS)-FPMPApp] is a potent and selective inhibitor of HIV-1 reverse transcriptase but not of HSV-1 DNA polymerase or DNA polymerase .alpha.. (RS)-FPMPApp, akin to PMEa diphosphate (PMEApp), acts as a DNA chain terminator. The DNA chain-terminating properties of PMEApp and (RS)-FPMPApp seem to be a prerequisite for acyclic nucleoside phosphonates to exhibit antiretrovirus (i.e., anti-HIV) activity.

L13 ANSWER 79 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 129532-77-0 REGISTRY

CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]phosphonic acid (9CI) (CA INDEX NAME)

OTHER NAMES:

CN PMEa diphosphate

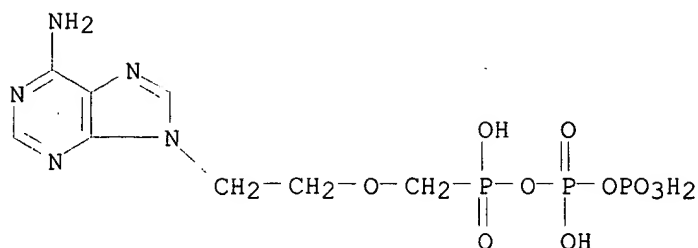
FS 3D CONCORD

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SR CA

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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

27 REFERENCES IN FILE CA (1967 TO DATE)

27 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:173722 Metal ion-binding properties of the antiviral nucleotide analogue 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA). Why is its diphosphorylated form, PMEApp4-, initially a better substrate for nucleic acid polymerases than (2'-deoxy)-adenosine 5-triphosphate (dATP4-/ATP4). Sigel, Helmut (Inst. of Inorganic Chemistry, Univ. of Basel, Basel, CH-4056, Switz.). Pure and Applied Chemistry, 71(9), 1727-1740 (English) 1999. CODEN: PACHAS. ISSN: 0033-4545. Publisher: Blackwell Science Ltd..

AB A review and discussion with 55 refs. The metal ion-coordinating properties (Mg2+, Mn2+, Zn2+, etc. = M2+) are summarized for (i) the dianion of 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA2- = adenine (9)-CH2CH2-O-CH2-PO32-) and (ii) methylphosphonylphosphate (MePP3- = CH3P(O)2--O-PO32-). The obsd. increased stability of the M(PMEA) complexes is mostly due to the formation of five-membered chelates involving the ether oxygen of the -CH2-O-CH2-PO32- residue; with some metal ions (Ni2+, Cu2+) in addn. an interaction with N3 of the adenine residue occurs. The M(MePP)- complexes are also somewhat more stable than those of diphosphate monoesters, like Me diphosphate, because of the enhanced basicity of the phosphonyl unit. These two observations provide an explanation for the fact that diphosphorylated PMEApp4-, an analog of (d)ATP4-, is initially a better substrate for several nucleic acid polymerases than dATP4-. The higher basicity of the phosphonyl group and the formation of the five-membered chelates favor PMEApp4- over dATP4- because they facilitate the M(.alpha.)-M(.beta.,.gamma.) coordination pattern needed for the enzyme-catalyzed incorporation of the substrate in the growing nucleic acid chain.

REFERENCE 2: 132:58689 9-(2-Phosphonylmethoxyethyl) derivatives of purine nucleotide analogs: A comparison of their metabolism and interaction with cellular DNA synthesis. Kramata, Pavel; Downey, Kathleen M. (Gilead Sciences, Foster City, CA, USA). Molecular Pharmacology, 56(6), 1262-1270 (English) 1999. CODEN: MOPMA3. ISSN: 0026-895X. Publisher: American Society for Pharmacology and Experimental Therapeutics.

AB Incubation of CEM cells for 24 h with the guanine, 2,6-diaminopurine, and adenine nucleotide analogs of the 9-(2-phosphonylmethoxyethyl) series, 9-(2-phosphonylmethoxyethyl)guanine (PMEG), 9-(2-phosphonylmethoxyethyl)-2,6-diaminopurine (PMEDAP), and 9-(2-phosphonylmethoxyethyl)adenine (PMEA), was found to inhibit DNA synthesis 50% at concns. of 1, 6, and 25 .mu.M, resp. Possible reasons for the marked differences were investigated, including cellular transport of the analogs, different efficiencies of intracellular phosphorylation, differential effects on 2'-deoxynucleotide (dNTP) pools, and differences in the affinities of the

cellular DNA polymerases for the diphosphate derivs. of the drugs. No significant differences in cellular uptake were found among the analogs; however, they did differ in the efficiency of phosphorylation, i.e., CEM cells were found to accumulate higher levels of PMEG-diphosphate (PMEGpp) than PMEDAP-diphosphate (PMEDApp) or PMEA-diphosphate (PMEApp). Treatment of cells with any of the nucleotide analogs resulted in increased dNTP pools, with PMEG producing the greatest increase. All three analogs had the greatest effect on the dATP pool size, whereas the dGTP pool size was not significantly affected. Comparison of the ratios of nucleotide analog diphosphates to their corresponding dNTPs under conditions where DNA synthesis is inhibited 50% suggested that cellular DNA polymerases were approx. twice as sensitive to PMEGpp than to PMEDApp and 5-fold more sensitive to PMEGpp than to PMEApp. Consistent with this hypothesis, examn. of the efficiencies with which the replicative DNA polymerases .alpha., .delta., and .epsilon. incorporated the analogs showed that DNA polymerase .delta., the most sensitive of the DNA polymerases, incorporated PMEGpp twice as efficiently as PMEDApp and 7-fold more efficiently than PMEApp.

REFERENCE 3: 131:237529 Effect of acyclic nucleoside phosphonates on the HIV-1 integrase in vitro. Abu, Sheika G.; Tramontano, E.; Loi, A. G.; Franchetti, P.; Grifantini, M.; La Colla, P. (Dipartimento di Scienze Chimiche, Universita di Camerino, Camerino, 62032, Italy). Nucleosides & Nucleotides, 18(4 & 5), 849-851 (English) 1999. CODEN: NUNUD5. ISSN: 0732-8311. Publisher: Marcel Dekker, Inc..

AB Integrase (IN) is an essential enzyme in the human immunodeficiency virus type-1 (HIV-1) replication cycle and, thus, a potential target for chemotherapeutic agents. Because various nucleotide analogs have been reported to inhibit IN in vitro, we investigated the effect of acyclic nucleoside phosphonates. Both unphosphorylated and diphosphorylated derivs. were inhibitory to IN at concns. ranging between 60 and 800 .mu.M, with diphosphorylated derivs. being 5- to 8-fold more potent than unphosphorylated counterparts.

REFERENCE 4: 131:210795 9-[2-(phosphonomethoxy)ethyl]adenine diphosphate (PMEApp) as a substrate toward replicative DNA polymerases .alpha., .delta., .epsilon., and .epsilon.*. Birkus, Gabriel; Votruba, Ivan; Holy, Antonin; Otova, Berta (Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague, 16610/6, Czech Rep.). Biochemical Pharmacology, 58(3), 487-492 (English) 1999. CODEN: BCPCA6. ISSN: 0006-2952. Publisher: Elsevier Science Inc..

AB The diphosphoryl deriv. of the acyclic nucleotide phosphonate analog 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA), found previously to weakly inhibit DNA pol .delta./proliferating cell nuclear antigen, was studied as a substrate for pol .alpha., .delta., .epsilon., and .epsilon.*. A comparison of the Vmax and Km for this deriv. (PMEApp) and dATP demonstrated that the relative efficiency of the incorporation of this analog into the DNA chain is decreasing in the following order: pol .delta. .simeq. pol .epsilon. .simeq. pol .epsilon.* > pol .alpha.. Under the reaction conditions, this incorporation amounted to 4.4 to 0.7% of dAMP mols. Similar Km values for PMEApp and dATP in pol .epsilon. and pol .epsilon.* catalyzed reactions revealed that proteolysis of the enzyme probably does not affect the dNTP binding site. The DNA polymerases tested were inhibited by the reaction product (PMEA terminated DNA chain) with similar Ki/Km ratios (pol .alpha. 0.2; pol .delta., 0.1; pol .epsilon. 0.05; and pol .epsilon.*, 0.06). The assocd. 3'-5'-exonuclease activity of pol .delta., .epsilon., and .epsilon.* was able to excise PMEA from the 3'-OH end of DNA with a rate one order of magnitude lower than that of the dAMP residue.

REFERENCE 5: 131:99168 Why is the antiviral nucleotide analog 9-[2-(phosphonomethoxy)ethyl]adenine in its diphosphorylated form

(PMEApp4-) initially a better substrate for polymerases than (2'-deoxy)adenosine 5'-triphosphate (dATP4-/ATP4-)? Considerations on the mechanism of nucleic acid polymerases. Sigel, Helmut; Song, Bin; Blindauer, Claudia A.; Kapinos, Larisa E.; Gregan, Fridrich; Pronayova, Nadja (Institute of Inorganic Chemistry, University of Basel, Basel, Switz.). Chemical Communications (Cambridge) (8), 743-744 (English) 1999. CODEN: CHCOFS. ISSN: 1359-7345. Publisher: Royal Society of Chemistry.

AB The observation that the antivirally active PMEApp4- in its diphosphorylated form (PMEApp4-) is initially a better substrate for polymerases than dATP4- (ATP4-) can be rationalized by (i) the increased basicity of the phosphonyl group (compared to a phosphoryl group) and (ii) the participation of the ether O atom of PMEApp4- in metal ion binding; both effects together favor M2+ binding at the .alpha. group and thus its nucleophilic attack.

REFERENCE 6: 130:119131 A 6-basepair insert in the reverse transcriptase gene of human immunodeficiency virus type 1 confers resistance to multiple nucleoside inhibitors. Winters, Mark A.; Coolley, Kristi L.; Girard, Yvette A.; Levee, Darcy J.; Hamdan, Hasnah; Shafer, Robert W.; Katzenstein, David A.; Merigan, Thomas C. (Center for AIDS Research at Stanford, Stanford University, Stanford, CA, 94305-5107, USA). Journal of Clinical Investigation, 102(10), 1769-1775 (English) 1998. CODEN: JCINAO. ISSN: 0021-9738. Publisher: Rockefeller University Press.

AB While many point mutations in the HIV-1 reverse transcriptase (RT) confer resistance to antiretroviral drugs, inserts or deletions in this gene have not been previously characterized. In this report, 14 RT inhibitor-treated patients were found to have HIV-1 strains possessing a 6-basepair insert between codons 69 and 70 of the RT gene. Known drug resistance mutations were also obsd. in these strains, with T215Y appearing in all strains. Genotypic anal. indicated that the inserts had substantial nucleotide variability that resulted in relatively restricted sets of amino acid sequences. Linkage of patients' treatment histories with longitudinal sequencing data showed that insert strains appeared during drug regimens contg. ddI or ddC, with prior or concurrent AZT treatment. Drug susceptibility tests of recombinant patient isolates showed reduced susceptibility to nearly all nucleoside RT inhibitors. Site-directed mutagenesis studies confirmed the role of the inserts alone in conferring reduced susceptibility to most RT inhibitors. The addn. of AZT-assocd. drug resistance mutations further increased the range and magnitude of resistance. These results establish that inserts, like point mutations, are selected in vivo during antiretroviral therapy and provide resistance to multiple nucleoside analogs.

REFERENCE 7: 128:162555 In vitro characterization of the anti-human cytomegalovirus activity of PMEApp4- (Adefovir). Xiong, Xiaofeng; Flores, Carmina; Fuller, Michael D.; Mendel, Dirk B.; Mulato, Andrew S.; Moon, Keith; Chen, Ming S.; Cherrington, Julie M. (Gilead Sciences, Foster City, CA, 94404, USA). Antiviral Research, 36(2), 131-137 (English) 1997. CODEN: ARSRDR. ISSN: 0166-3542. Publisher: Elsevier Science B.V..

AB PMEApp4- {9-[2-(phosphonomethoxy)ethyl]adenine;} has shown anti-cytomegalovirus activity in animal models and in preliminary human trials. PMEApp4- diphosphate (PMEApp4-), the active antiviral metabolite of PMEApp4-, is a potent inhibitor of human cytomegalovirus (HCMV) DNA polymerase. PMEApp4- is efficiently taken up and phosphorylated to PMEApp4- in numerous human cell lines. In vitro replication of wild type and drug resistant HCMV clin. isolates is effectively inhibited by PMEApp4-. PMEApp4- in combination with other anti-HCMV agents shows additive inhibition of HCMV replication.

REFERENCE 8: 127:171038 Intracellular metabolism and action of acyclic nucleoside phosphonates on DNA replication. Pisarev, Vladimir M.; Lee, Suk-Hee; Connelly, Michele C.; Fridland, Arnold (Department of Infectious

Diseases, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA). Mol. Pharmacol., 52(1), 63-68 (English) 1997. CODEN: MOPMA3. ISSN: 0026-895X. Publisher: Williams & Wilkins.

- AB 9-(2-Phosphonylmethoxyethyl)guanine (PMEG) is an acyclic nucleoside phosphonate deriv. that has demonstrated significant anticancer activity in a no. of in vitro and in vivo animal model systems. In this study, we compared the cellular metab. of PMEG and 9-(2-phosphonylmethoxyethyl)adenine (PMEA), a clin. active anti-HIV and antihepatitis agent, and the inhibitory activities of their putative active diphosphate derivs., PMEGpp and PMEApp, resp., toward human cellular DNA polymerases. PMEG was significantly more cytotoxic than PMEA against a panel of human leukemic cells. The diphosphate derivs. were the major metabolites formed in cells on both these agents, with PMEGpp reaching cellular concn. approx. 4-fold higher than that achieved for PMEApp. These differences in cellular accumulation of the diphosphate derivs. were not, however, sufficient to account for the 30-fold difference in cytotoxicity between the two analogs. PMEGpp was also at least a 7-fold more effective inhibitor of in vitro simian vacuolating virus 40 DNA replication system than that of PMEApp (IC₅₀ = 4.6 .mu.M). Studies with a defined primed DNA template showed that PMEGpp was a potent inhibitor of both human polymerases .alpha. and .delta., two key enzymes involved in cellular DNA replication, whereas PMEApp inhibited these enzymes relatively poorly. From these studies, we can conclude that the factors that contribute to the enhanced antileukemic activity of PMEG derives both from its increased anabolic phosphorylation and the increased potency of the diphosphate deriv. to target the cellular replicative DNA polymerases.

REFERENCE 9: 127:144785 (S)-1-(3-Hydroxy-2-phosphonylmethoxypropyl)cytosine (HPMPC) inhibits HIV-1 replication in epithelial cells, but not T-lymphocytes. Srinivas, Ranga V.; Connely, Michele; Fridland, Arnold (Dep. Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA). Antiviral Research, 35(1), 23-27 (English) 1997. CODEN: ARSRDR. ISSN: 0166-3542. Publisher: Elsevier.

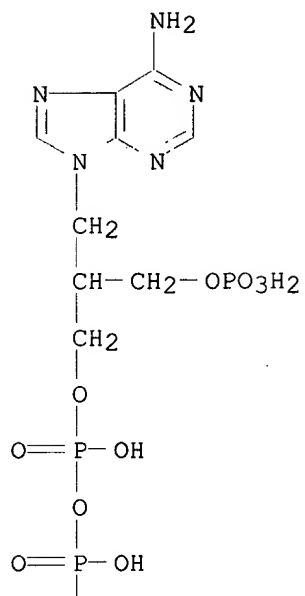
- AB PMEA [9-(2-phosphonylmethoxyethyl)adenine] inhibited both HSV-1 and HIV-1 replication in MT-2 and HeLa-CD4 cells. (S)-1-[3-hydroxy-2-(phosphonylmethoxy)propyl]cytosine (HPMPC) inhibited both these viruses in the epithelioid HeLa-CD4 cells, but did not inhibit either virus in the T-lymphocytic MT-2 cells. PMEA and HPMPC are metabolized to their diphosphorylated forms within cells, which then inhibit viral polymerases. We therefore compared the metab. of PMEA and HPMPC in MT-2 and HeLa-CD4 cells. PMEApp formation was efficient in both the cell types, whereas HPMPCpp levels were .apprx.3-10 fold lower in MT-2 cells, compared to HeLa-CD4 cells. These results indicate that HPMPC can inhibit HIV replications in the appropriate cell types, and show that differences in their metab. cannot account entirely for the lack of antiviral efficacy of HPMPC in MT-2 cells.

REFERENCE 10: 127:44485 The thiocarboxanilides UC-10 and UC-781 have an additive inhibitory effect against human immunodeficiency virus type 1 reverse transcriptase and replication in cell culture when combined with other antiretroviral drugs. Balzarini, J.; De Clercq, E. (Rega Inst. Medical Res., Katholieke Univ. Leuven, Louvain, B-3000, Belg.). Antiviral Chemistry & Chemotherapy, 8(3), 197-204 (English) 1997. CODEN: ACCHEH. ISSN: 0956-3202. Publisher: International Medical Press.

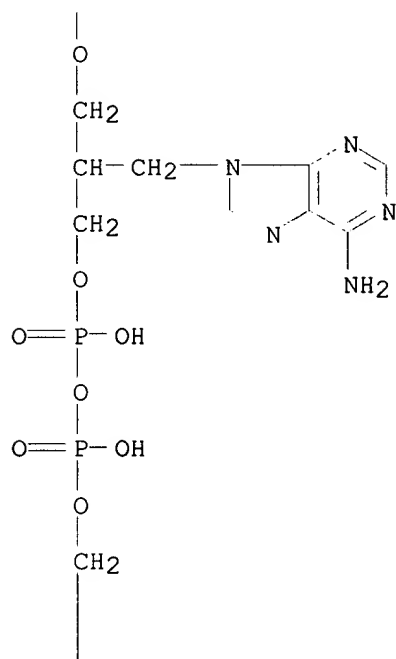
- AB The thiocarboxanilides represent a structural class of potent and selective human immunodeficiency virus type 1 (HIV-1)-specific reverse transcriptase (RT) inhibitors. Combinations of the clin. candidate thiocarboxanilides UC-10 (oxime ether deriv.) and UC-781 (pentenyloxy ether deriv.) with a variety of nucleoside RT inhibitors (NRTIs) and non-nucleoside RT inhibitors (NNRTIs), two HIV protease inhibitors and one fusion/uncoating inhibitor were evaluated for their inhibitory effects on

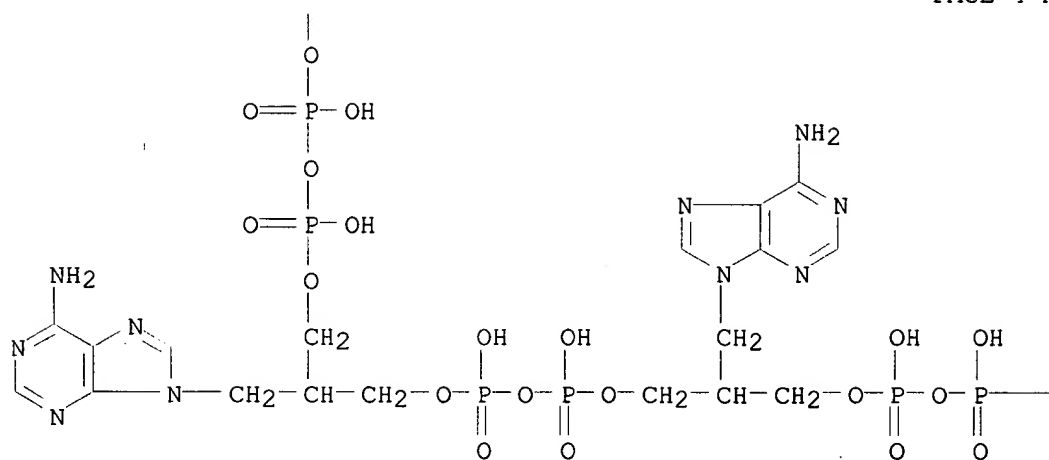
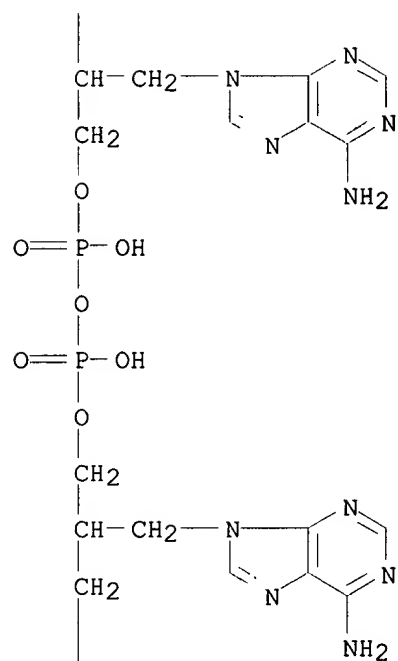
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L13 ANSWER 80 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 121712-89-8 REGISTRY
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CN Diphosphoric acid, P,P'-bis[2,10,18,26,34-pentakis[(6-amino-9H-purin-9-yl)methyl]-5,7,13,15,21,23,29,31,37,37-decahydroxy-4,6,8,12,14,16,20,22,24,28,30,32,36-tridecaoxa-5,7,13,15,21,23,29,31,37-nonaphosphaheptatriacont-1-yl] ester, bis(P'',P''',P'''',P''''',P''''',P''''',P''''',P''''',P''''')-oxide)
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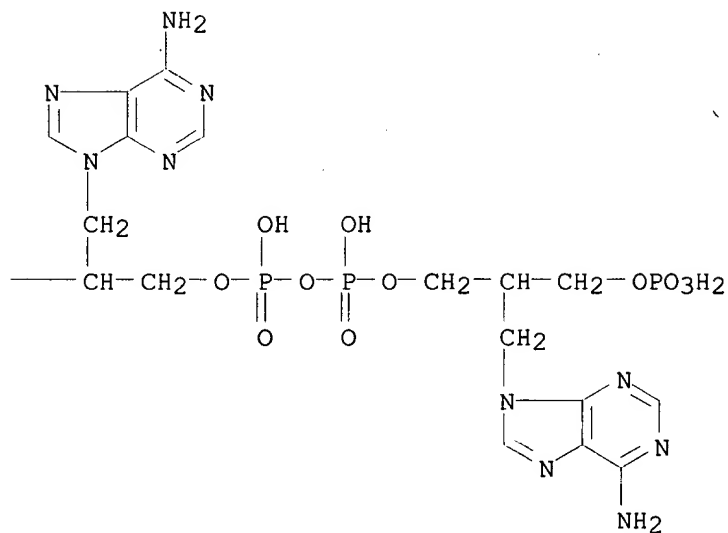
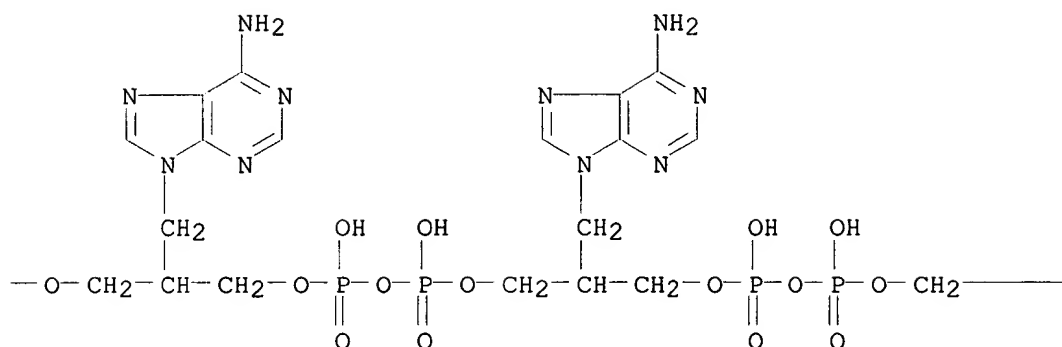
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PAGE 2-A







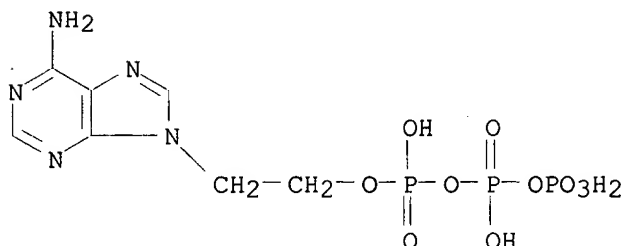
1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:52604 Some acyclic analogs of nucleotides and their template-directed reactions. Tohidi, Mahrokh; Orgel, Leslie E. (Salk Inst. Biol. Stud., San Diego, CA, 92138, USA). J. Mol. Evol., 28(5), 367-73 (English) 1989. CODEN: JMEVAU. ISSN: 0022-2844.

AB Bismonophosphoimidazolides of acyclic analogs of guanosine and adenosine were synthesized. They undergo oligomerization in the presence of complementary polynucleotide templates. Details of their synthesis and their subsequent template- and nontemplate-directed reactions are described, and their possible relevance to the origin of life is discussed.

L13 ANSWER 81 OF 166 REGISTRY COPYRIGHT 2002 ACS
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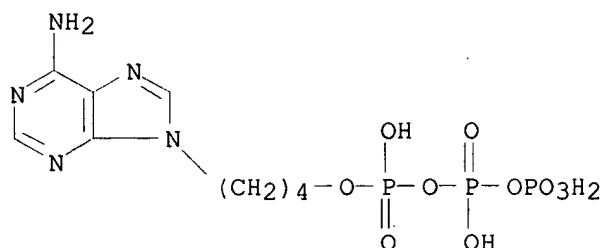
● 4 Na

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:58238 Synthesis and biological evaluation of ATP analogs acting at putative purinergic P2X-receptors (on the guinea pig bladder). Howson, William; Taylor, Edwin Michael; Parsons, Michael Edward; Novelli, Riccardo; Wilczynska, Maria Alkksandra; Harris, Deborah Tracy (Dep. Med. Chem., Smith, Kline and French Res. Ltd., Welwyn/Hertfordshire, AL6 9AR, UK). Eur. J. Med. Chem., 23(5), 433-9 (English) 1988. CODEN: EJMCA5. ISSN: 0223-5234.

AB Potency of .apprx.25 ATP analogs as P2x agonists relative to ATP were detd. Of these 7 ATP analogs were prepd. by known chem. methods. Optimization of the pharmacol. exptl. technique enabled reproducible responses to ATP to be obtained in the 0.2-100 .mu.M concn. range and the potencies of ATP analogs relative to ATP to be accurately detd. Alterations of the three main parts of the ATP mol., i.e., the triphosphate, ribose and base, suggest that the triphosphate group is responsible for the efficacy of the agonist, whereas the ribose and adenine moieties are assocd. with affinity.

L13 ANSWER 82 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 121683-03-2 REGISTRY
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1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:58238 Synthesis and biological evaluation of ATP analogs acting at putative purinergic P2X-receptors (on the guinea pig bladder). Howson, William; Taylor, Edwin Michael; Parsons, Michael Edward; Novelli, Riccardo; Wilczynska, Maria Alkksandra; Harris, Deborah Tracy (Dep. Med. Chem., Smith, Kline and French Res. Ltd., Welwyn/Hertfordshire, AL6 9AR, UK). Eur. J. Med. Chem., 23(5), 433-9 (English) 1988. CODEN: EJMCA5. ISSN: 0223-5234.

AB Potency of .apprx.25 ATP analogs as P2x agonists relative to ATP were detd. Of these 7 ATP analogs were prepd. by known chem. methods. Optimization of the pharmacol. exptl. technique enabled reproducible responses to ATP to be obtained in the 0.2-100 .mu.M concn. range and the potencies of ATP analogs relative to ATP to be accurately detd. Alterations of the three main parts of the ATP mol., i.e., the triphosphate, ribose and base, suggest that the triphosphate group is responsible for the efficacy of the agonist, whereas the ribose and adenine moieties are assocd. with affinity.

L13 ANSWER 83 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 121683-02-1 REGISTRY

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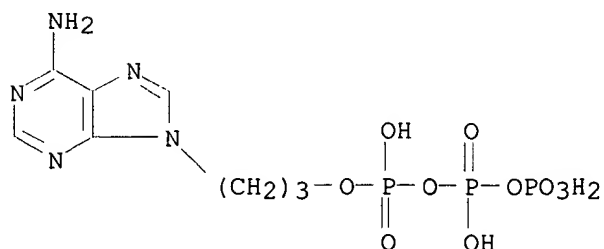
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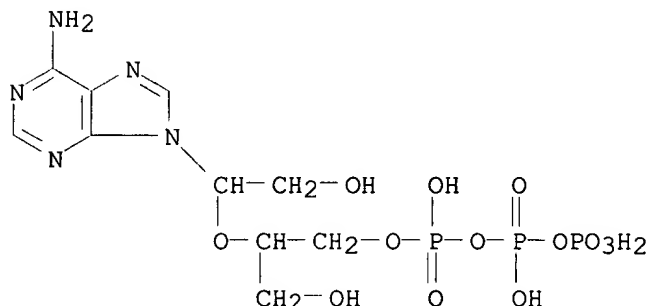
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1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:58238 Synthesis and biological evaluation of ATP analogs acting at putative purinergic P2X-receptors (on the guinea pig bladder). Howson, William; Taylor, Edwin Michael; Parsons, Michael Edward; Novelli, Riccardo; Wilczynska, Maria Alkksandra; Harris, Deborah Tracy (Dep. Med. Chem., Smith, Kline and French Res. Ltd., Welwyn/Hertfordshire, AL6 9AR, UK). Eur. J. Med. Chem., 23(5), 433-9 (English) 1988. CODEN: EJMCA5. ISSN: 0223-5234.

AB Potency of .apprx.25 ATP analogs as P2x agonists relative to ATP were detd. Of these 7 ATP analogs were prepd. by known chem. methods. Optimization of the pharmacol. exptl. technique enabled reproducible responses to ATP to be obtained in the 0.2-100 .mu.M concn. range and the potencies of ATP analogs relative to ATP to be accurately detd. Alterations of the three main parts of the ATP mol., i.e., the triphosphate, ribose and base, suggest that the triphosphate group is responsible for the efficacy of the agonist, whereas the ribose and adenine moieties are assocd. with affinity.

L13 ANSWER 84 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 120083-53-6 REGISTRY
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2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:4281 Substrate specificity of T4 RNA ligase: influence of the ATP ribose moiety on AMP-RNA ligase covalent complex formation, studies on affinity of T4 RNA ligase. Juodka, B. A.; Labeikyte, D. Ja.; Sabaliauskiene, V. L. (Dep. Biochemistry Biophysics, Faculty Natural Sciences, Vilnius University, Vilnius, 2009, Lithuania). Biokhimiya (Moscow), 60(3), 478-84 (Russian) 1995. CODEN: BIOHAO. ISSN: 0320-9725.

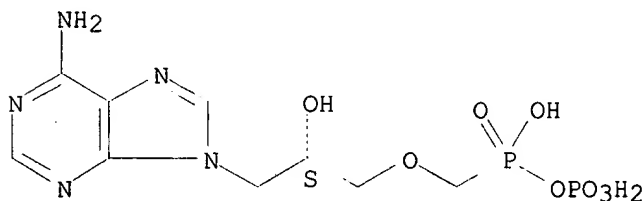
AB To elucidate the role of the ribose moiety in substrate binding, various ATP derivs. modified in ribose moiety were studied as probes for the T4 RNA ligase first stage reaction. The kinetic parameters for competitive inhibition were detd. Inhibition expts. using substrate analogs demonstrated that the major binding determinants of ATP analogs were

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purine and triphosphate moieties of ATP; modification of the ribose moiety was not crit. Adenosine triphosphates attached to agarose were used as affinity adsorbent for purifn. of T4 RNA ligase. These derivs. had been successfully used in reversible binding of the enzyme. Best results were achieved with agarose coupled via N6 of the purine moiety of ATP.

- REFERENCE 2: 110:170508 Gorging response of *Glossina palpalis palpalis* to ATP analogs. Galun, R.; Kabayo, J. P. (Entomol. Unit, Jt. FAO/IAEA Programme, Seibersdorf, A-2444, Austria). *Physiol. Entomol.*, 13(4), 419-23 (English) 1988. CODEN: PENTDE. ISSN: 0307-6962.
- AB The potencies of seventeen analogs of ATP as gorging inducers for *G. palpalis palpalis* were evaluated. The ranking for ED that induced half the flies to gorge (ED50) was: adenosine 5'-tetraphosphate .gtoreq. ATP = 2'-deoxyadenosine 5'-triphosphate .gtoreq. ADP = 2'-deoxyadenosine 5'-diphosphate > .beta., .gamma.-imidoadenosine 5'-triphosphate > 3'-deoxyadenosine 5'-triphosphate .gtoreq. 2',3'-dideoxyadenosine 5'-triphosphate > .beta., .gamma.-methyleneadenosine 5'-triphosphate > ATP 2',3'-dialdehyde > .alpha., .beta.-methyleneadenosine 5'-triphosphate >>AMP.
- L13 ANSWER 85 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 116454-96-7 REGISTRY
 CN Isophosphoric acid, [[3-(6-amino-9H-purin-9-yl)-2-hydroxypropoxy]methyl]-, trilithium salt, (S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C9 H15 N5 O8 P2 . 3 Li
 SR CA
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
 (*File contains numerically searchable property data)

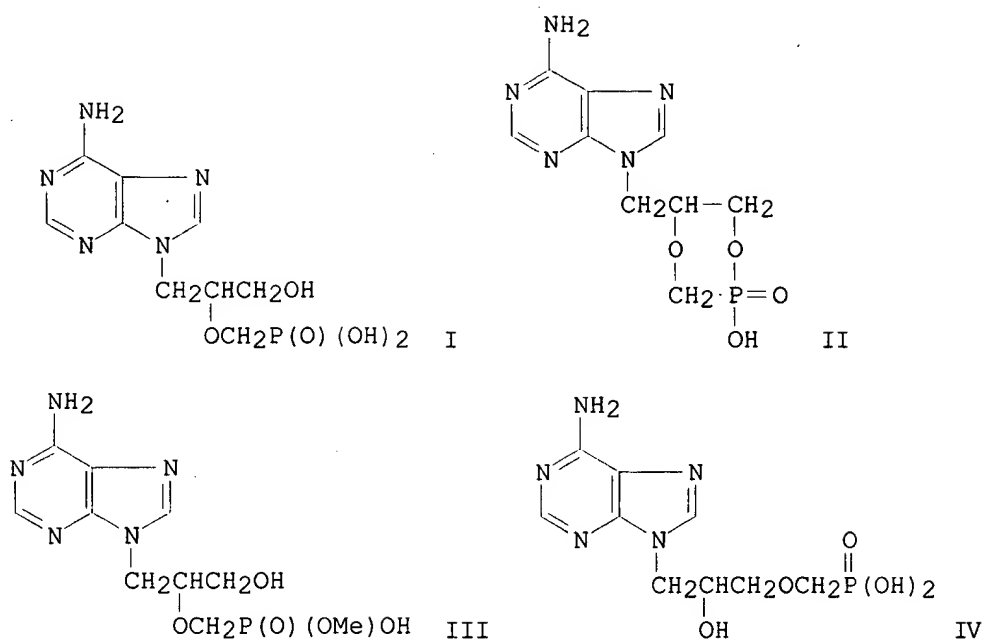
Absolute stereochemistry.



● 3 Li

- 1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

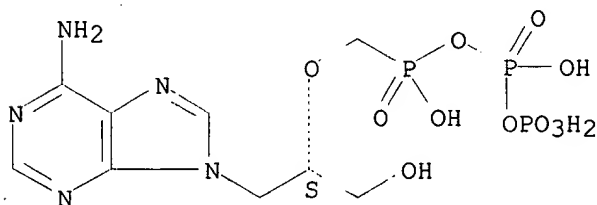
- REFERENCE 1: 109:149953 Acyclic nucleotide analogs. Part II. Synthesis of potential prodrugs and metabolites of 9-(S)-(3-hydroxy-2-phosphonylmethoxypropyl)adenine. Rosenberg, Ivan; Holy, Antonin (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10/6, Czech.). *Collect. Czech. Chem. Commun.*, 52(11), 2792-800 (English) 1987. CODEN: CCCCAK. ISSN: 0366-547X.
- GI



AB Cyclic and acyclic esters of the title compd. (I) were prepd. as potential prodrugs. For example, I was treated with N,N'-dicyclohexylcarbodiimide to give 89% cyclic phosphonate II. Treatment of (RS)-II with MeONa gave 80% Me ester (RS)-III. Similar reactions were also carried out with acyclic nucleotide analog IV.

L13 ANSWER 86 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 116454-95-6 REGISTRY
 CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)-1-(hydroxymethyl)ethoxy]methyl]phosphonic acid trilithium salt, (S)- (9CI)
 (CA INDEX NAME)
 FS STEREOSEARCH
 MF C9 H16 N5 O11 P3 . 3 Li
 SR CA
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
 (*File contains numerically searchable property data)
 CRN (111964-44-4)

Absolute stereochemistry.



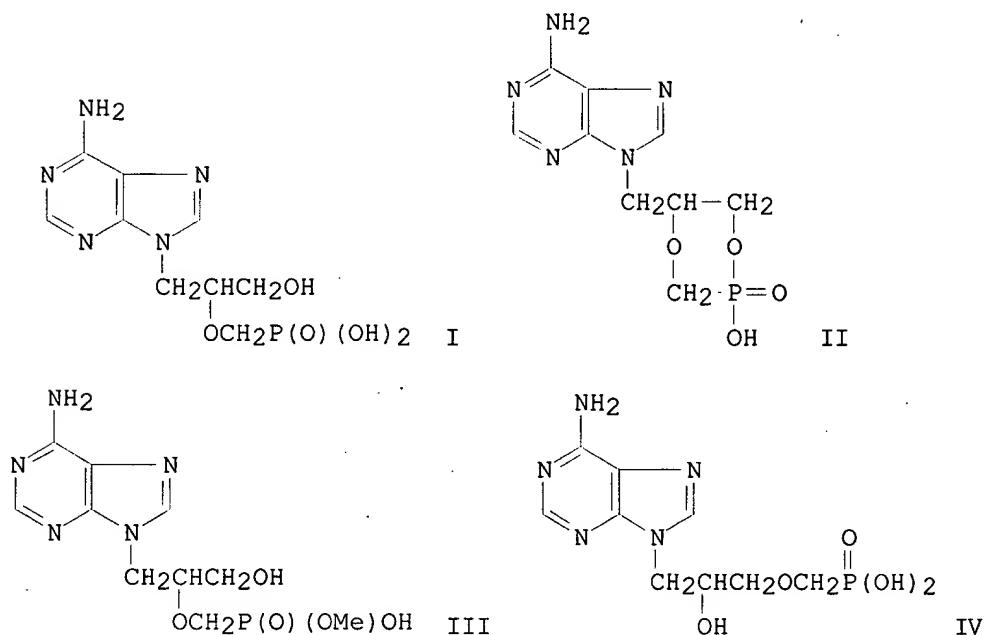
3 Li

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

REFERENCE 1: 109:149953 Acyclic nucleotide analogs. Part II. Synthesis of potential prodrugs and metabolites of 9-(S)-(3-hydroxy-2-phosphonylmethoxypropyl)adenine. Rosenberg, Ivan; Holy, Antonin (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10/6, Czech.). Collect. Czech. Chem. Commun., 52(11), 2792-800 (English) 1987. CODEN: CCCCAK. ISSN: 0366-547X.

GI



AB Cyclic and acyclic esters of the title compd. (I) were prepd. as potential prodrugs. For example, I was treated with *N,N'*-dicyclohexylcarbodiimide to give 89% cyclic phosphonate II. Treatment of (RS)-II with MeONA gave 80% Me ester (RS)-III. Similar reactions were also carried out with acyclic nucleotide analog IV.

L13 ANSWER 87 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 116454-94-5 REGISTRY

CN Isohypophosphoric acid, [[2-(6-amino-9H-purin-9-yl)-1-(hydroxymethyl)ethoxy]methyl]-, trilithium salt, (S)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C9 H15 N5 O8 P2 . 3 Li

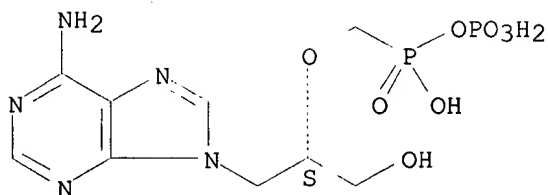
SR CA

LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT

(*File contains numerically searchable property data)

CRN (111964-43-3)

Absolute stereochemistry.



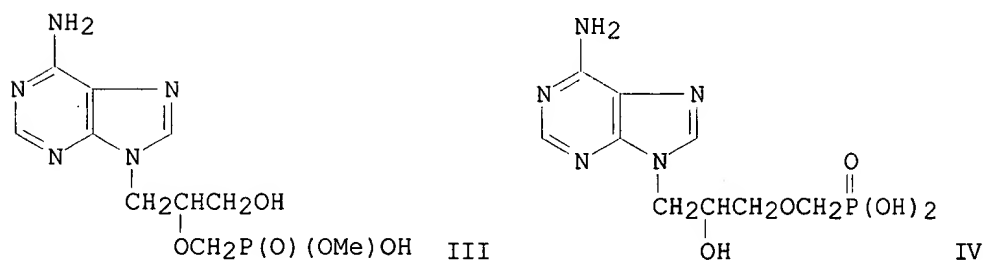
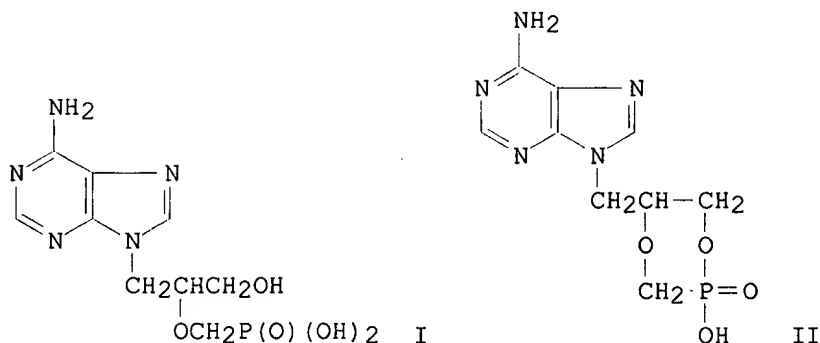
●3 Li

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 109:149953 Acyclic nucleotide analogs. Part II. Synthesis of potential prodrugs and metabolites of 9-(S)-(3-hydroxy-2-phosphonylmethoxypropyl)adenine. Rosenberg, Ivan; Holy, Antonin (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10/6, Czech.). Collect. Czech. Chem. Commun., 52(11), 2792-800 (English) 1987. CODEN: CCCCAK. ISSN: 0366-547X.

GI



AB Cyclic and acyclic esters of the title compd. (I) were prepd. as potential prodrugs. For example, I was treated with N,N'-dicyclohexylcarbodiimide to give 89% cyclic phosphonate II. Treatment of (RS)-II with MeONA gave 80% Me ester (RS)-III. Similar reactions were also carried out with acyclic nucleotide analog IV.

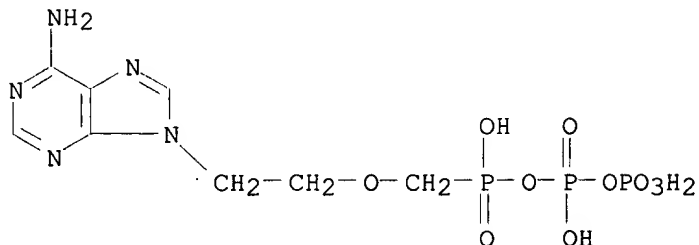
L13 ANSWER 88 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 116384-62-4 REGISTRY

CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-

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yl)ethoxy)methyl]phosphonic acid, lithium salt (9CI) (CA INDEX NAME)
 MF C8 H14 N5 O10 P3 . x Li
 SR CA
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
 (*File contains numerically searchable property data)
 CRN (129532-77-0)

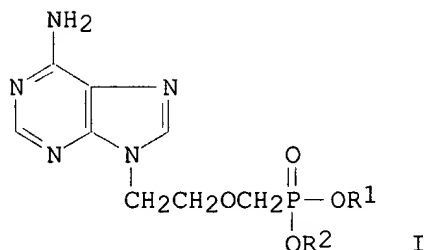


● x Li

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 109:129559 Acyclic nucleotide analogs. Part III. Synthesis of 9-(2-phosphonylmethoxyethyl)adenine and related compounds. Holy, Antonin; Rosenberg, Ivan (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10/6, Czech.). Collect. Czech. Chem. Commun., 52(11), 2801-9 (English) 1987. CODEN: CCCCAK. ISSN: 0366-547X.

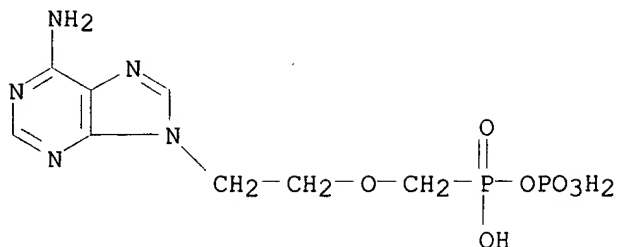
GI



AB Adenine was treated with NaH in DMF and then with RCH2CH2OCH2P(O)(OEt)2 (R = Cl, Br, p-MeC6H4SO3), to give 46-64% acyclic nucleotide analog I (R1 = R2 = Et), which was treated with Me3SiBr in MeCN to give 73% title compd. [I; R1 = R2 = H (II)]. II was converted to the diphosphate I [R1 = P(O)(OH)2, R2 = H] and triphosphate I [R1 = P(O)(OH)OP(O)(OH)2, R2 = H] via phosphorylation of its morpholide.

L13 ANSWER 89 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 116384-61-3 REGISTRY
 CN Isophosphoric acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]-, lithium salt (9CI) (CA INDEX NAME)
 MF C8 H13 N5 O7 P2 . x Li
 SR CA
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
 (*File contains numerically searchable property data)
 CRN (129556-87-2)

Searched by: Mary Hale 308-4258 CM-1 12D16

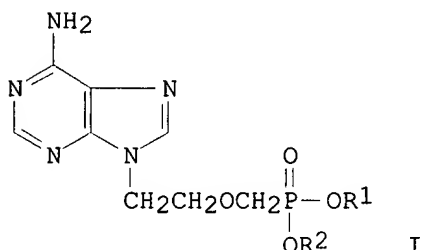


●x Li

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 109:129559 Acyclic nucleotide analogs. Part III. Synthesis of 9-(2-phosphonylmethoxyethyl)adenine and related compounds. Holy, Antonin; Rosenberg, Ivan (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10/6, Czech.). Collect. Czech. Chem. Commun., 52(11), 2801-9 (English) 1987. CODEN: CCCCAK. ISSN: 0366-547X.

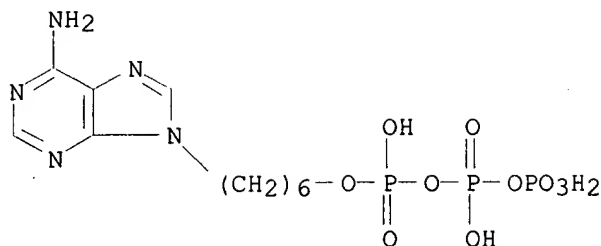
GI



AB Adenine was treated with NaH in DMF and then with $\text{RCH}_2\text{CH}_2\text{OCH}_2\text{P}(\text{O})(\text{OEt})_2$ ($\text{R} = \text{Cl}, \text{Br}, \text{p-MeC}_6\text{H}_4\text{SO}_3$), to give 46-64% acyclic nucleotide analog I ($\text{R}_1 = \text{R}_2 = \text{Et}$), which was treated with Me_3SiBr in MeCN to give 73% title compd. [I; $\text{R}_1 = \text{R}_2 = \text{H}$ (II)]. II was converted to the diphosphate I [$\text{R}_1 = \text{P}(\text{O})(\text{OH})_2$, $\text{R}_2 = \text{H}$] and triphosphate I [$\text{R}_1 = \text{P}(\text{O})(\text{OH})\text{OP}(\text{O})(\text{OH})_2$, $\text{R}_2 = \text{H}$] via phosphorylation of its morpholide.

L13 ANSWER 90 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 114191-83-2 REGISTRY
CN Triphosphoric acid, P-[6-(6-amino-9H-purin-9-yl)hexyl] ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C11 H20 N5 O10 P3
SR CA
LC STN Files: CA, CAPLUS

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 108:182489 Characterization of the ATP4- receptor that mediates permeabilization of rat mast cells. Tatham, Peter E. R.; Cusack, Noel J.; Gomperts, Bastien D. (Dep. Exp. Pathol., Univ. Coll. London, London, WC1E 6JJ, UK). Eur. J. Pharmacol., 147(1), 13-21 (English) 1988. CODEN: EJPHAZ. ISSN: 0014-2999.

AB ATP (as the tetrabasic acid, ATP4-) applied externally to rat mast cells causes the formation of lesions which permit influx and efflux of low-mol.-wt., normally impermeant aq. solutes. Membrane permeabilization was monitored with 2 fluorescent dyes, ethidium which stains the nucleus, and 1-(4-trimethylammoniumphenyl)-6-phenyl-1,3,5-hexatriene which stains the cytosolic surfaces of intracellular membranes following entry into the cells. Permeabilization by ATP is not affected by the metabolic status of the cells, and is maintained at temps. as low as 8.degree.. The ability of 30 structural analogs of ATP to effect mast cell permeabilization were tested. The analogs include those having substituents in the 2- and 8-positions of the purine ring, structural and optical isomers of the ribose sugar, and variations in the triphosphate chain. The pattern of selectivity displayed by the rat mast cell ATP4- receptor is distinct from those characteristic of the P1 purinoceptor for adenosine and the P2X and P2Y purinoceptors for adenine nucleotides.

L13 ANSWER 91 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 112968-03-3 REGISTRY

CN Tetraphosphoric acid, P,P'''-bis[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, tetrasodium salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Tetraphosphoric acid, P,P'''-bis[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, tetrasodium salt, [2R-[1[R*(R*)],2R*(R*)]]-

FS STEREOSEARCH

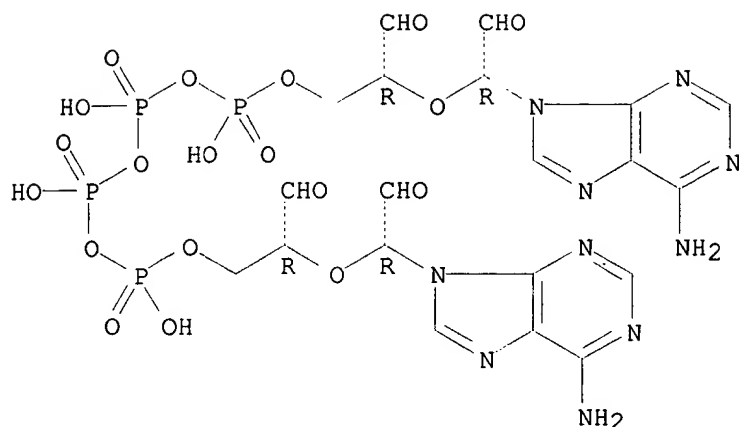
MF C20 H24 N10 O19 P4 . 4 Na

SR CAS Registry Services

LC STN Files: CHEMCATS

CRN (75042-77-2)

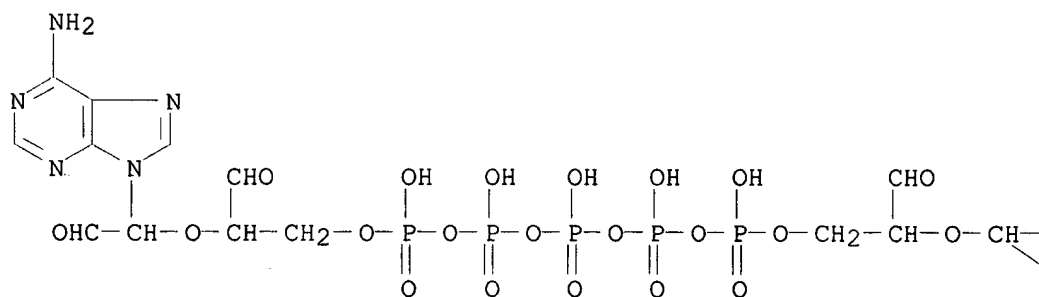
Absolute stereochemistry.



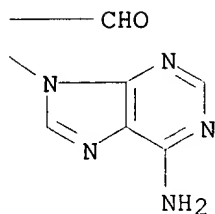
● 4 Na

L13 ANSWER 92 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 112966-12-8 REGISTRY
 CN Pentaphosphoric acid, P,P''''-bis[2-oxoethoxy]-3-oxopropyl ester, pentasodium salt (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Pentaphosphoric acid, P,P''''-bis[2-oxoethoxy]-3-oxopropyl ester, pentasodium salt, [2R-[1[R*(R*)],2R*(R*)]]-
 MF C20 H25 N10 O22 P5 . 5 Na
 SR CAS Registry Services
 LC STN Files: ANABSTR, CHEMCATS
 CRN (107148-01-6)

PAGE 1-A



● 5 Na



L13 ANSWER 93 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 112897-98-0 REGISTRY

CN Triphosphoric acid, P,P''-bis[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, trisodium salt (9CI) (CA INDEX NAME)

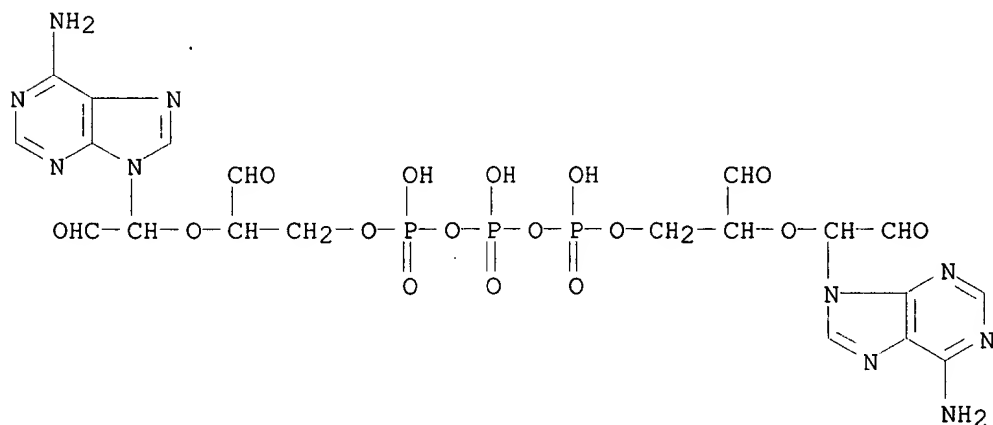
OTHER CA INDEX NAMES:

CN Triphosphoric acid, P,P''-bis[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, trisodium salt, [2R-[1[R*(R*)],2R*(R*)]]-

MF C20 H23 N10 O16 P3 . 3 Na

SR CAS Registry Services

LC STN Files: CHEMCATS



● 3 Na

L13 ANSWER 94 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 111964-44-4 REGISTRY

CN Diphosphoric acid, monoanhydride with [[(1S)-2-(6-amino-9H-purin-9-yl)-1-(hydroxymethyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)

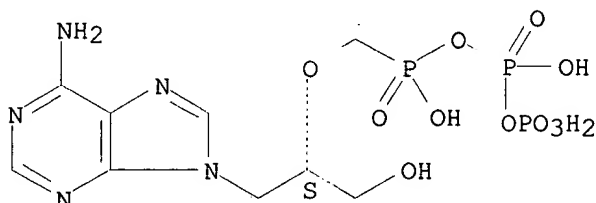
OTHER CA INDEX NAMES:

CN Diphosphoric acid, monoanhydride with [[2-(6-amino-9H-purin-9-yl)-1-

Searched by: Mary Hale 308-4258 CM-1 12D16

(hydroxymethyl)ethoxy)methyl]phosphonic acid, (S)-
 FS STEREOSEARCH
 MF C9 H16 N5 O11 P3
 CI COM
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

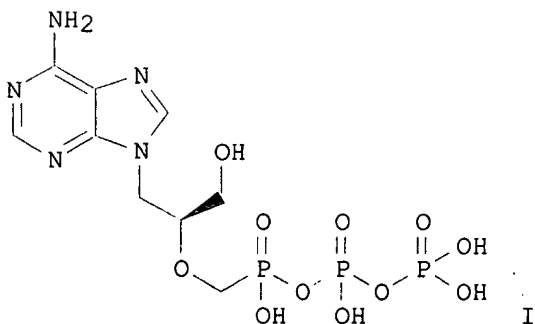
10 REFERENCES IN FILE CA (1967 TO DATE)
 10 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:73888 An alternative synthesis of HPMPC and HMPA diphosphoryl derivatives. Otmar, Miroslav; Votruba, Ivan; Holy, Antonin (Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague, 166 10, Czech Rep.). Collection Symposium Series, 2(Chemistry of Nucleic Acid Components), 252-254 (English) 1999. CODEN: CSYSFN. Publisher: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic.

AB A symposium report. The authors have synthesized the triphosphonate of (S)-1-(3-hydroxy-2-phosphonomethoxypropyl)cytosine via a morpholidate activated intermediate using dimethoxytrityl as a hydroxy-protecting group.

REFERENCE 2: 133:70555 HPMPApp as a substrate toward replicative DNA polymerases .alpha., .delta. and .epsilon.. Birkus, Gabriel; Votruba, Ivan; Holy, Antonin; Otova, Berta (Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague, 166 10, Czech Rep.). Collection Symposium Series, 2(Chemistry of Nucleic Acid Components), 289-293 (English) 1999. CODEN: CSYSFN. Publisher: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic.

GI



AB The diphosphoryl deriv. (S)-9-(3-hydroxy-2-phosphonomethoxypropyl)adenine diphosphate (HPMPApp, I) of the acyclic nucleoside phosphonate analog HPMPA was studied as a substrate for pol .alpha., .delta. and .epsilon.. The relative efficiency of incorporation of the analog into two different synthetic template-primers compared to the natural substrate dATP decreases in the order: .epsilon. > pol .delta. > pol .alpha., whereas the substrate activity of HPMPApp is approx. 5 to 24 times lower than that for dATP.

REFERENCE 3: 125:268990 Structural features of acyclic nucleotide analogs conferring inhibitory effects on cellular replicative DNA polymerases. Kramata, Pavel; Birkus, Gabriel; Otmar, Miroslav; Votruba, Ivan; Holy, Antonin (Institute Organic Chemistry Biochemistry, Academy Sciences Czech Republic, Prague, 166 10, Czech Rep.). Collect. Czech. Chem. Commun., 61(Spec. Issue), S188-S191 (English) 1996. CODEN: CCCCAK. ISSN: 0010-0765.

AB Diphosphates of phosphonomethoxyalkyl acyclic nucleotide analogs were tested as inhibitors of two proteolyzed forms of cellular repetitive DNA polymerase .epsilon., and DNA polymerases .alpha. and .delta.. The Ki/Km ratios are given. Effects of different substitutions on their inhibitory activity are discussed.

REFERENCE 4: 125:104413 Different inhibitory potencies of acyclic phosphonomethoxyalkyl nucleotide analogs toward DNA polymerases .alpha., .delta., and .epsilon.. Kramata, Pavel; Votruba, Ivan; Otova, Berta; Holy, Antonin (Inst. of Organic Chemistry and Biochemistry, Acad. of Sci. of The Czech Republic, Prague, 16610, Czech Rep.). Mol. Pharmacol., 49(6), 1005-1011 (English) 1996. CODEN: MOPMA3. ISSN: 0026-895X.

AB Based on the powerful virustatic potency and cytostatic activity of adenine, 2,6-diaminopurine, and guanine derivs. of acyclic phosphonate nucleotide analog (S)-1-(3-hydroxy-2-phosphonomethoxypropyl) and 9-(2-phosphonomethoxyethyl) series, we examd. the inhibitory potencies of their diphosphates [(S)-9-(3-hydroxy-2-phosphonomethoxypropyl)adenine diphosphate (HPMPApp), 9-(2-phosphonomethoxyethyl)adenine diphosphate, 9-(2-phosphonomethoxyethyl)-2,6-diaminopurine diphosphate (PMEDAPpp), and 9-(2-phosphonomethoxyethyl)guanine diphosphate, analogs of nucleoside 5'-triphosphate] toward cellular DNA polymerases .alpha., .delta., and .epsilon. (isolated from tumors of T cell spontaneous acute lymphoblastic leukemia in Sprague-Dawley inbred rats). Kinetic measurements (Km, Ki, and Vmax) of synthetic homopolymeric template primers have shown that HPMPApp is a selective and potent inhibitor of polymerase .epsilon., whereas PMEDAPpp strongly inhibits polymerase .delta.. These two compds. may be useful for elucidating the roles of polymerases .delta. and .epsilon.. Of the nucleotide analogs tested, 9-(2-phosphonomethoxyethyl)guanine diphosphate is the most efficient inhibitor of polymerases .alpha. and .epsilon., whereas the diphosphate of 9-(2-phosphonomethoxyethyl)adenine, the therapeutically important agent adefovir, inhibits polymerases .alpha. and .epsilon. relatively poorly and exerts only moderate inhibition of polymerase .delta.. These data are quite consistent with previously reported cytostatic activity of these nucleotide analogs. All of the enzymes studied catalyze the incorporation of 9-(2-phosphonomethoxyethyl)adenine, 9-(2-phosphonomethoxyethyl)-2,6-diaminopurine, and (S)-9-3-hydroxy-2-(phosphonomethoxypropyl)adenine into DNA chain. 9-(2-Phosphonomethoxyethyl)adenine diphosphate and PMEDAPpp were confirmed to be DNA chain terminators. HPMPApp formed poly(dT)/oligo(dA18)-[(S)-9-(3-hydroxy-2-phosphonomethoxypropyl)adenine]2-4 structures.

REFERENCE 5: 118:93736 Phosphorylation of 9-(2-phosphonomethoxyethyl)adenine and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine by AMP(dAMP) kinase

from L1210 cells. Merta, Ales; Votruba, Ivan; Jindrich, Jindrich; Holy, Antonin; Cihlar, Tomas; Rosenberg, Ivan; Otmar, Miroslav; Herve, Tchaou Y. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Biochem. Pharmacol., 44(10), 2067-77 (English) 1992. CODEN: BCPCA6. ISSN: 0006-2952.

- AB The acyclic nucleotide analogs 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), which display potent antiviral activity, are transformed in the cells to their mono- and diphosphoryl derivs. The enzyme that in 2 steps phosphorylates PMEA and HPMPA to their diphosphoryl derivs. was purified from mouse L1210 cells. The enzyme co-purified with AMP (dAMP) kinase activity; the best substrates of this enzyme were AMP, ADP, and dAMP. Other nucleoside 5'-triphosphates or creatine phosphate could not be substituted for ATP as a phosphate donor. At least one other enzyme (creatine kinase) can transform the monophosphoryl derivs. of the studied compds. to their resp. diphosphates.

REFERENCE 6: 115:89025 Inhibition of the growth of Plasmodium falciparum and Plasmodium berghei by the DNA polymerase inhibitor HPMPA. De Vries, Erik; Stam, Jeanette G.; Franssen, Frits F. J.; Nieuwenhuijs, Hans; Chavalitschewinkoon, Porntip; De Clercq, Erik; Overdulve, J. Prosper; Van der Vliet, Peter C. (Lab. Physiol. Chem., Univ. Utrecht, Utrecht, 3521 GG, Neth.). Mol. Biochem. Parasitol., 47(1), 43-50 (English) 1991. CODEN: MBIPDP. ISSN: 0166-6851.

- AB The acyclic adenosine analog (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA) belongs to a class of nucleoside analogs originally described as having potent activity against a broad spectrum of DNA viruses. The effects of this class of drugs on the growth of cultured P. falciparum were examd. Strong inhibition was obsd. by HPMPA (ID50 = 47 nM) at concns. >1000-fold less than the cytotoxic dose for human cells. 3-Deaza-HPMPA was even more strongly inhibitory (ID50 = 8 nM), whereas several other acyclic nucleosides were not effective. In mice infected with P. berghei, increase of parasitemia can be blocked for 4-6 days by a single injection of HPMPA. Repeated drug administration blocks parasite growth for prolonged periods at doses that are clin. feasible. Also detd. was the inhibition of several purified Plasmodium DNA polymerases by diphosphorylated HPMPA (HPMPApp). DNA polymerase .alpha.-like enzymes of P. falciparum and P. berghei are inhibited with an IC50 = 40 .mu.M and a .gamma.-like DNA polymerase from P. falciparum is even 40-fold more sensitive to the drug. The inhibition by HPMPApp is competitive with dATP, strongly suggesting that Plasmodium DNA polymerases are targets for this class of nucleotide analog.

REFERENCE 7: 113:184251 Phosphonylmethyl ethers of acyclic nucleoside analogs: inhibitors of HSV-1 induced ribonucleotide reductase. Cerny, Jaroslav; Votruba, Ivan; Vonka, Vladimir; Rosenberg, Ivan; Otmar, Miroslav; Holy, Antonin (Inst. Org. Chem. Biochem., Slovak Acad. Sci., Prague, 16610/6, Czech.). Antiviral Res., 13(5), 253-63 (English) 1990. CODEN: ARSRDR. ISSN: 0166-3542.

- AB Diphosphates of N-(S)-(3-hydroxy-2-phosphonylmethoxypropyl) (HPMP) and N-(2-phosphonylmethoxyethyl) (PME) derivs. of purine and pyrimidine heterocyclic bases inhibit HSV-1 encoded ribonucleotide reductase. Of the compds. studied, the most efficient inhibitors of CDP redn. (at 5.1 .mu.mol/L) by the HSV-1-encoded enzyme are HPMPApp (IC50 = 0.9 .mu.mol/L) and PMEApp (IC50 = 8 .mu.mol/L). PMEApp does not inhibit the enzyme isolated from the mutant HSV-1 KOS strain which is resistant to PMEA at a concn. of 100 .mu.g/mL. The enzyme isolated from the PMEA-resistant virus strain is also sensitive to inhibitory effects of hydroxyurea and HPMPApp. Thus, the inhibitory potency of HPMPApp and PMEApp toward HSV-1 encoded ribonucleotide reductase might be connected with the anti-HSV activity of HPMPA and PMEA.

REFERENCE 8: 113:144780 Phosphorylation of acyclic nucleotide analogs HPMPA and PMEA in L1210 mouse leukemia cell extracts. Merta, A.; Vesely, J.; Votruba, I.; Rosenberg, I.; Holy, A. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Neoplasma, 37(2), 111-20 (English) 1990. CODEN: NEOLA4. ISSN: 0028-2685.

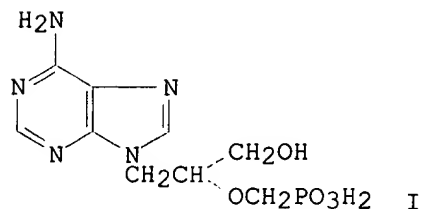
AB Acyclic nucleotide analogs, (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA) and 9-(2-phosphonylmethoxyethyl)adenine (PMEA), were phosphorylated in the presence of ribonucleoside 5'-triphosphates by the crude ext. from mouse leukemia cells L1210 affording the resp. mono- and diphosphoryl derivs. The donor efficiency was decreasing in the order CTP > UTP > ATP > GTP. The presence of an ATP regenerating system stimulated considerably the conversion of both compds. The rate of PMEA phosphorylation was 5-times slower than that of HPMPA both with and without an ATP regenerating system.

REFERENCE 9: 112:91268 Mechanism of inhibition of adenovirus DNA replication by the acyclic nucleoside triphosphate analog (S)-HPMPApp: influence of the adenovirus DNA binding protein. Mul, Yvonne M.; Van Miltenburg, Rob T.; De Clercq, Erik; Van der Vliet, Peter C. (Lab. Physiol. Chem., Univ. Utrecht, Utrecht, 3521 GG, Neth.). Nucleic Acids Res., 17(22), 8917-29 (English) 1989. CODEN: NARHAD. ISSN: 0305-1048.

AB The acyclic adenosine analog (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine [(S)-HPMPA] is a potent and selective inhibitor of adenovirus (Ad) replication in cell culture. The mechanism of inhibition was studied by using a reconstituted in vitro DNA replication system.. The diphosphoryl deriv. (S)-HPMPApp, but not (S)-HPMPA, inhibited DNA replication by origin-contg. fragments. The inhibitory effect was exerted at the level of elongation, while initiation was resistant to the drug. The elongation of short strands was only slightly impaired, while inhibition was maximal on synthesis of long DNA fragments. (S)-HPMPApp appeared to be competitive with dATP, suggesting that the Ad DNA polymerase is the prime target for the drug. The Ad DNA polymerase complexed with the precursor terminal protein was purified to homogeneity from cells infected with overproducing recombinant vaccinia viruses. With the use of gapped DNA or poly(dT).oligo(dA) templates, only a weak inhibition was obsd. However, inhibition was strongly enhanced in the presence of the adenovirus DNA-binding protein (DBP). Apparently, the increased polymn. reaction in the presence of DBP leads to increased drug sensitivity.

REFERENCE 10: 108:15846 Intracellular phosphorylation of broad-spectrum anti-DNA virus agent (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine and inhibition of viral DNA synthesis. Votruba, Ivan; Bernaerts, Ria; Sakuma, Takashi; De Clercq, Erik; Merta, Ales; Rosenberg, Ivan; Holy, Antonin (Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.). Mol. Pharmacol., 32(4), 524-9 (English) 1987. CODEN: MOPMA3. ISSN: 0026-895X.

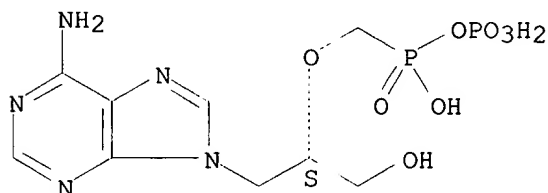
GI



AB The acyclic nucleotide analog (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine [(S)-HPMPA] (I) potently and selectively inhibited the replication of herpes simplex virus type 1 (HSV-1). Radiolabeled (S)-[U-14C-adenine]HPMP was investigated, and its metab. by HSV-1-infected and mock-infected cells were investigated. The drug was taken up by the cells and subsequently converted to its monophosphoryl and diphosphoryl derivs. by cellular enzymes. It was incorporated to a very low extent into DNA of both mock-infected and HSV-1-infected Vero cells. (S)-HPMPA inhibited HSV-1 DNA synthesis at a concn. that is several orders of magnitude lower than the concn. required for inhibition of cellular DNA synthesis. Thus, the selectivity of (S)-HPMPA as an antiviral agent cannot be attributed to a different phosphorylation by virus-infected or uninfected cells but resides in a specific inhibitory effect on viral DNA synthesis.

L13 ANSWER 95 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 111964-43-3 REGISTRY
 CN Isohypophosphoric acid, [[2-(6-amino-9H-purin-9-yl)-1-(hydroxymethyl)ethoxy]methyl]-, (S)- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C9 H15 N5 O8 P2
 CI COM
 SR CA
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)
 5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 118:93736 Phosphorylation of 9-(2-phosphonomethoxyethyl)adenine and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine by AMP(dAMP) kinase from L1210 cells. Merta, Ales; Votruba, Ivan; Jindrich, Jindrich; Holy, Antonin; Cihlar, Tomas; Rosenberg, Ivan; Otmar, Miroslav; Herve, Tchaou Y. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Biochem. Pharmacol., 44(10), 2067-77 (English) 1992. CODEN: BCPCA6. ISSN: 0006-2952.

AB The acyclic nucleotide analogs 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 9-(S)-(3-hydroxy-2-phosphonomethoxypropyl)adenine (HPMPA), which display potent antiviral activity, are transformed in the cells to their mono- and diphosphoryl derivs. The enzyme that in 2 steps phosphorylates PMEA and HPMPA to their diphosphoryl derivs. was purified from mouse L1210 cells. The enzyme co-purified with AMP (dAMP) kinase activity; the best substrates of this enzyme were AMP, ADP, and dAMP. Other nucleoside 5'-triphosphates or creatine phosphate could not be substituted for ATP as a phosphate donor. At least one other enzyme (creatine kinase) can transform the monophosphoryl derivs. of the studied compds. to their resp. diphosphates.

REFERENCE 2: 115:63946 5-Phosphoribosyl 1-pyrophosphate synthetase converts

Searched by: Mary Hale 308-4258 CM-1 12D16

the acyclic nucleoside phosphonates 9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine and 9-(2-phosphonylmethoxyethyl)adenine directly to their antivirally active diphosphate derivatives. Balzarini, Jan; De Clercq, Erik (Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.). J. Biol. Chem., 266(14), 8686-9 (English) 1991. CODEN: JBCHA3. ISSN: 0021-9258.

- AB The acyclic nucleoside phosphonates 9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA) and 9-(2-phosphonylmethoxyethyl)adenine (PMEA) are potent inhibitors of DNA viruses and retroviruses, resp. Unlike nucleoside triphosphates, the metabolically active diphosphorylated forms of HPMPA and PMEA (designed HPMPApp and PMEApp) are synthesized in a reversible reaction in which the pyrophosphate group of 5-phosphoribosyl-1-pyrophosphate (PRPP) is directly transferred to HPMPA and PMEA by purified PRPP synthetase. PRPP synthetase does not act stereospecifically in that it recognizes both the S-enantiomer and the R-enantiomer of HPMPA as substrate. PRPP synthetase also recognizes other acyclic adenine and 2,6-diaminopurine riboside phosphonates as substrate. It is now imperative to evaluate the potential role of PRPP synthetase, as activating enzyme, in the antiviral action of this type of mol. in intact cells.

REFERENCE 3: 113:184251 Phosphonylmethyl ethers of acyclic nucleoside analogs: inhibitors of HSV-1 induced ribonucleotide reductase. Cerny, Jaroslav; Votruba, Ivan; Vonka, Vladimir; Rosenberg, Ivan; Otmar, Miroslav; Holy, Antonin (Inst. Org. Chem. Biochem., Slovak Acad. Sci., Prague, 16610/6, Czech.). Antiviral Res., 13(5), 253-63 (English) 1990. CODEN: ARSRDR. ISSN: 0166-3542.

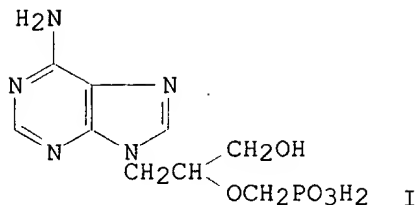
- AB Diphosphates of N-(S)-(3-hydroxy-2-phosphonylmethoxypropyl) (HPMP) and N-(2-phosphonylmethoxyethyl) (PME) derivs. of purine and pyrimidine heterocyclic bases inhibit HSV-1 encoded ribonucleotide reductase. Of the compds. studied, the most efficient inhibitors of CDP redn. (at 5.1 .mu.mol/L) by the HSV-1-encoded enzyme are HPMPApp (IC₅₀ = 0.9 .mu.mol/L) and PMEApp (IC₅₀ = 8 .mu.mol/L). PMEApp does not inhibit the enzyme isolated from the mutant HSV-1 KOS strain which is resistant to PMEA at a concn. of 100 .mu.g/mL. The enzyme isolated from the PMEA-resistant virus strain is also sensitive to inhibitory effects of hydroxyurea and HPMPApp. Thus, the inhibitory potency of HPMPApp and PMEApp toward HSV-1 encoded ribonucleotide reductase might be connected with the anti-HSV activity of HPMPA and PMEA.

REFERENCE 4: 113:144780 Phosphorylation of acyclic nucleotide analogs HPMPA and PMEA in L1210 mouse leukemia cell extracts. Merta, A.; Vesely, J.; Votruba, I.; Rosenberg, I.; Holy, A. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.). Neoplasma, 37(2), 111-20 (English) 1990. CODEN: NEOLA4. ISSN: 0028-2685.

- AB Acyclic nucleotide analogs, (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA) and 9-(2-phosphonylmethoxyethyl)adenine (PMEA), were phosphorylated in the presence of ribonucleoside 5'-triphosphates by the crude ext. from mouse leukemia cells L1210 affording the resp. mono- and diphosphoryl derivs. The donor efficiency was decreasing in the order CTP > UTP > ATP > GTP. The presence of an ATP regenerating system stimulated considerably the conversion of both compds. The rate of PMEA phosphorylation was 5-times slower than that of HPMPA both with and without an ATP regenerating system.

REFERENCE 5: 108:15846 Intracellular phosphorylation of broad-spectrum anti-DNA virus agent (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine and inhibition of viral DNA synthesis. Votruba, Ivan; Bernaerts, Ria; Sakuma, Takashi; De Clercq, Erik; Merta, Ales; Rosenberg, Ivan; Holy, Antonin (Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.). Mol. Pharmacol., 32(4), 524-9 (English) 1987. CODEN: MOPMA3.

GI



AB The acyclic nucleotide analog (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine [(S)-HPMPA] (I) potently and selectively inhibited the replication of herpes simplex virus type 1 (HSV-1). Radiolabeled (S)-[U-14C-adenine]HPMP was investigated, and its metab. by HSV-1-infected and mock-infected cells were investigated. The drug was taken up by the cells and subsequently converted to its monophosphoryl and diphosphoryl derivs. by cellular enzymes. It was incorporated to a very low extent into DNA of both mock-infected and HSV-1-infected Vero cells. (S)-HPMPA inhibited HSV-1 DNA synthesis at a concn. that is several orders of magnitude lower than the concn. required for inhibition of cellular DNA synthesis. Thus, the selectivity of (S)-HPMPA as an antiviral agent cannot be attributed to a different phosphorylation by virus-infected or uninfected cells but resides in a specific inhibitory effect on viral DNA synthesis.

L13 ANSWER 96 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 111647-41-7 REGISTRY

CN Triphosphoric acid, P-[2-{1-(6-amino-9H-purin-9-yl)-2-[[[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridinyl]methyl]amino]ethoxy]-3-hydroxypropyl] ester, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

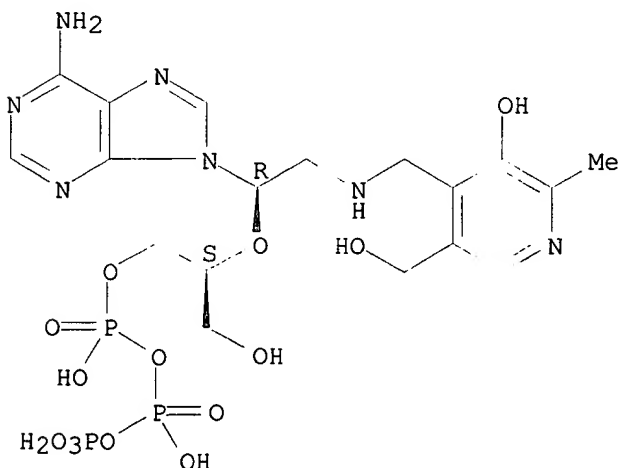
FS STEREOSEARCH

MF C18 H28 N7 O14 P3

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 107:232162 Brain pyridoxal kinase dissociation of the dimeric structure and catalytic activity of the monomeric species. Kwok, Francis; Scholz, Glen; Churchich, Jorge E. (Sch. Pharm., South Aust. Inst. Technol., Adelaide, Australia). Eur. J. Biochem., 168(3), 577-83 (English) 1987. CODEN: EJBCAI. ISSN: 0014-2956.

AB Reversible disocn. of the dimeric structure of brain pyridoxal kinase into subunits was attained by addn. of guanidinium-HCl (2M). The mol. mass of the subunits [40 kilodaltons (kDa)] was detd. by HPLC. Sepn. of the processes of refolding and assocn. of the monomeric species was achieved by attaching the protein subunits to a rigid matrix (Affi-gel 15). The matrix-bound monomer is catalytically competent. The reaction of the crosslinking reagent 4,4'-dimaleimidestilbene 2,2'-disulfonate (DMDS), a derivatized stilbene, with the dimeric structure of pyridoxal kinase resulted in the formation of an oligomeric species of 80 kDa detectable by SDS-PAGE. The crosslinked subunits exhibit the same catalytic parameters as the native enzyme. The presence of 2 nucleotide-binding sites per dimer was detd. by fluorimetric titrns. using pyridoxyl-ATP, a strong competitive inhibitor with respect to ATP. The ATP analog binds with a disocn. const. $K_d = 5 \mu\text{M}$ to each nucleotide site of the dimeric enzyme. The mode of binding pyridoxyl-ATP to the kinase is discussed in ref. to a model which assumes the presence of 2 binding domains per subunit.

L13 ANSWER 97 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 111625-58-2 REGISTRY

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-[[[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridinyl]methyl]amino]propyl] ester, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

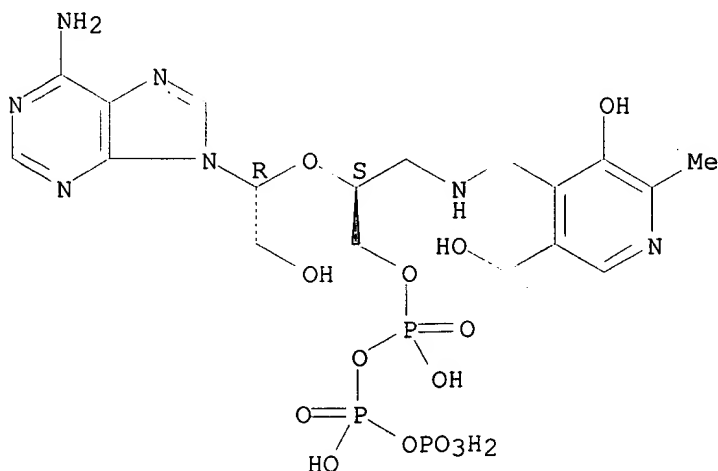
FS STEREOSEARCH

MF C18 H28 N7 O14 P3

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

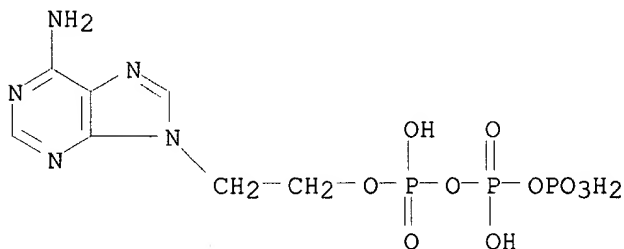
Searched by: Mary Hale 308-4258 CM-1 12D16

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 107:232162 Brain pyridoxal kinase dissociation of the dimeric structure and catalytic activity of the monomeric species. Kwok, Francis; Scholz, Glen; Churchich, Jorge E. (Sch. Pharm., South Aust. Inst. Technol., Adelaide, Australia). Eur. J. Biochem., 168(3), 577-83 (English) 1987. CODEN: EJBCAI. ISSN: 0014-2956.

AB Reversible dissocn. of the dimeric structure of brain pyridoxal kinase into subunits was attained by addn. of guanidinium-HCl (2M). The mol. mass of the subunits [40 kilodaltons (kDa)] was detd. by HPLC. Sepn. of the processes of refolding and assocn. of the monomeric species was achieved by attaching the protein subunits to a rigid matrix (Affi-gel 15). The matrix-bound monomer is catalytically competent. The reaction of the crosslinking reagent 4,4'-dimaleimidestilbene 2,2'-disulfonate (DMS), a derivatized stilbene, with the dimeric structure of pyridoxal kinase resulted in the formation of an oligomeric species of 80 kDa detectable by SDS-PAGE. The crosslinked subunits exhibit the same catalytic parameters as the native enzyme. The presence of 2 nucleotide-binding sites per dimer was detd. by fluorimetric titrns. using pyridoxyl-ATP, a strong competitive inhibitor with respect to ATP. The ATP analog binds with a dissocn. const. $K_d = 5 \mu\text{M}$ to each nucleotide site of the dimeric enzyme. The mode of binding pyridoxyl-ATP to the kinase is discussed in ref. to a model which assumes the presence of 2 binding domains per subunit.

L13 ANSWER 98 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 110475-69-9 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-, triphosphate, tetralithium salt (6CI) (CA INDEX NAME)
MF C7 H12 N5 O10 P3 . 4 Li
SR CAOLD
LC STN Files: CAOLD
CRN (55881-00-0)



●4 Li

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

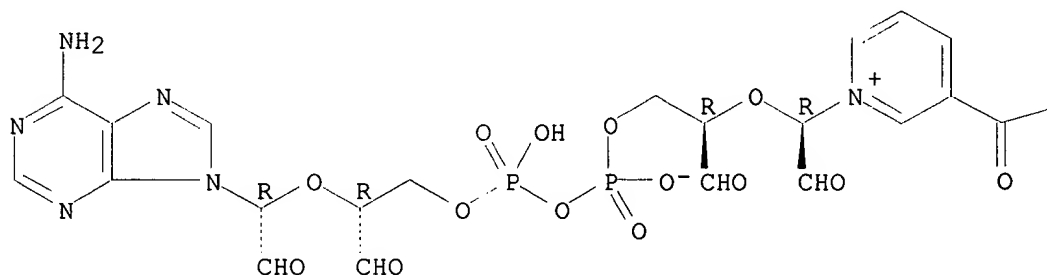
L13 ANSWER 99 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 108321-75-1 REGISTRY
CN Pyridinium, 3-(aminocarbonyl)-1-[(1R,3R,11R,13R)-13-(6-amino-9H-purin-9-yl)-1,3,11-triformyl-6,8-dihydroxy-6,8-dioxido-14-oxo-2,5,7,9,12-pentaoxa-6,8-diphosphatetradec-1-yl]-, inner salt, monosodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyridinium, 3-(aminocarbonyl)-1-[13-(6-amino-9H-purin-9-yl)-1,3,11,13-tetraformyl-6,8-dihydroxy-2,5,7,9,12-pentaoxa-6,8-diphosphatridec-1-yl]-,

Searched by: Mary Hale 308-4258 CM-1 12D16

inner salt, monosodium salt, P,P'-dioxide, [1R-(1R*,3R*,11R*,13R*)]-
 OTHER NAMES:
 CN Pyridinium, 3-(aminocarbonyl)-1-[13-(6-amino-9H-purin-9-yl)-1,3,11-triformyl-6,8-dihydroxy-6,8-dioxido-14-oxo-2,5,7,9,12-pentaoxa-6,8-diphosphatetradec-1-yl]-, inner salt, monosodium salt, [1R-(1R*,3R*,11R*,13R*)]-
 FS STEREOSEARCH
 MF C21 H23 N7 O14 P2 . Na
 SR CAS Registry Services
 LC STN Files: CA, CAPLUS
 CRN (75521-15-2)

Absolute stereochemistry.

PAGE 1-A



● Na

PAGE 1-B

—NH₂

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

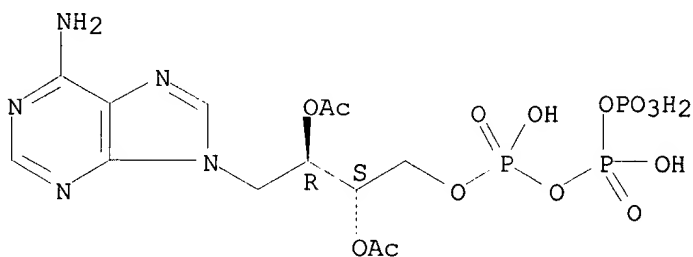
REFERENCE 1: 120:101198 Using periodate-oxidized nucleotide as affinity label for the nucleotide site of proteins. Lin, Chin Chun; Chang, Gu Gang (Dep. Biochem., Natl. Def. Med. Cent., Taipei, Taiwan). J. Protein Chem., 12(5), 627-32 (English) 1993. CODEN: JPCHD2. ISSN: 0277-8033.
 AB The active-site of pigeon liver malic enzyme was labeled with a fluorescent affinity label, the periodate-oxidized aminopyridine adenine dinucleotide phosphate. The modified enzyme was subjected to proteolytic digestion with trypsin. The resulted peptides were then sepd. with reversed-phase high-performance liq. chromatog. on Waters .mu.Bondapak C18 column. Two pure fluorescent peptides were obtained after three runs of the chromatog. The peptides were then subjected to automatic Edman degrdn. on a Beckman peptide sequencer and subsequently sepd. and identified with phenylthiohydantoin C18 column. No sequence was obtained. The possible reasons for the failure in sequencing the periodate-oxidized nucleotides labeled active site peptide and some possible pitfalls in using these reagents were discussed.

L13 ANSWER 100 OF 166 REGISTRY COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 12D16

RN 108267-43-2 REGISTRY
 CN Erythritol, 1-(6-amino-9H-purin-9-yl)-1-deoxy-, 2,3-diacetate
 4-triphosphate (7CI) (CA INDEX NAME)
 FS STEREOSEARCH
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 CI COM
 SR CAOLD
 LC STN Files: BEILSTEIN*, CAOLD
 (*File contains numerically searchable property data)

Absolute stereochemistry.

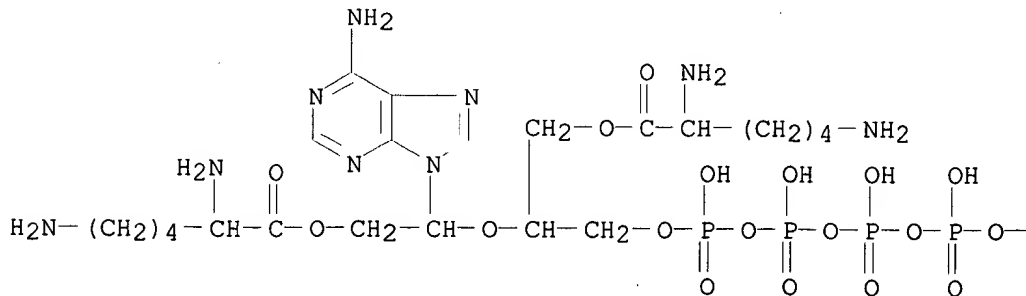


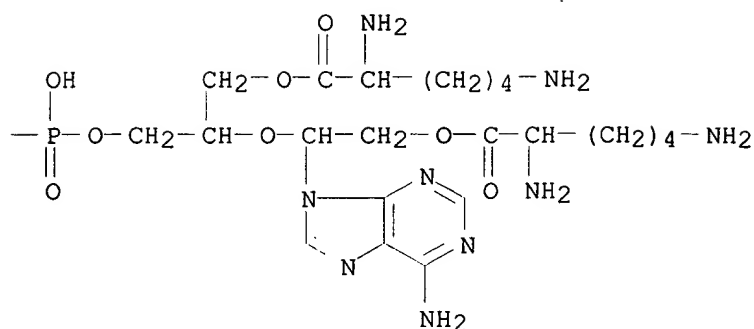
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L13 ANSWER 101 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 107173-86-4 REGISTRY
 CN L-Lysine, 2,16-bis[1-(6-amino-9H-purin-9-yl)-2-[(2,6-diamino-1-oxohexyl)oxy]ethoxy]-5,7,9,11,13-pentahydroxy-5,7,9,11,13-pentaoxido-4,6,8,10,12,14-hexaoxa-5,7,9,11,13-pentaphosphaheptadecane-1,17-diyl ester, [2S-[2R*[S*(R*)],16R*[S*(R*)]]]- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN L-Lysine, 2,16-bis[1-(6-amino-9H-purin-9-yl)-2-[(2,6-diamino-1-oxohexyl)oxy]ethoxy]-5,7,9,11,13-pentahydroxy-4,6,8,10,12,14-hexaoxa-5,7,9,11,13-pentaphosphaheptadecane-1,17-diyl ester, P,P',P'',P''',P''''-pentaoxide, [2S-[2R*[S*(R*)],16R*[S*(R*)]]]-
 MF C44 H81 N18 O26 P5
 SR CA
 LC STN Files: CA, CAPLUS

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 106:151984 Biochemistry of terminal deoxynucleotidyltransferase (TdT): characterization and mechanism of inhibition of TdT by P1,P5-bis(5'-adenosyl) pentaphosphate. Pandey, Virendranath; Modak, Mukund J. (New Jersey Med. Sch., Univ. Med. Dent. New Jersey, Newark, NJ, 07103, USA). Biochemistry, 26(7), 2033-8 (English) 1987. CODEN: BICHAW. ISSN: 0006-2960.

AB The catalysis of DNA synthesis of calf thymus TdT was strongly inhibited in the presence of Ap5A, whereas replicative DNA polymerases from mammalian, bacterial, and oncornaviral sources were totally insensitive to Ap5A addn. The Ap5A-mediated inhibition of TdT appeared to occur via its interaction at both the substrate-binding and primer-binding domains as judged by (a) classical competitive inhibition plots with respect to both substrate deoxynucleoside triphosphate (dNTP) and DNA primer and (b) inhibition of UV light-mediated crosslinking of substrate dNTP and oligomeric DNA primer to their resp. binding sites. Further kinetic analyses of Ap5A inhibition revealed that the dissocn. const. of the Ap5A-enzyme complex, with either substrate binding or primer binding domain participating in the complex formation, was .apprx.6-fold higher ($K_i = 1.5 \mu\text{M}$) compared to the dissocn. const. ($K_i = 0.25 \mu\text{M}$) of the Ap5A-TdT complex when both domains were available for binding. In order to study the binding stoichiometry of Ap5A to TdT, an oxidized deriv. of Ap5A, which exhibited identical inhibitory properties as its parent compd., was employed. The oxidn. product of Ap5A, presumably a tetraaldehyde deriv., bound irreversibly to TdT when inhibitor-enzyme complex was subjected to borohydride redn. The presence of aldehyde groups in the oxidized Ap5A appeared essential for inhibitory activity since its redn. to alc. via borohydride redn. or its linkage to free amino acids prior to use as an inhibitor rendered it completely ineffective. With use of a tritiated oxidn. product of Ap5A, a binding stoichiometry of 1 mol of Ap5A to 1 mol of TdT was obsd. Thus, a single Ap5A mol. appears to span across both the substrate and primer binding site domains in TdT.

L13 ANSWER 102 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 107148-04-9 REGISTRY

CN L-Arginine, 2,16-bis[2-[[2-amino-5-[(aminoiminomethyl)amino]-1-oxopentyl]oxy]-1-(6-amino-9H-purin-9-yl)ethoxy]-5,7,9,11,13-pentahydroxy-

5,7,9,11,13-pentaoxido-4,6,8,10,12,14-hexaoxa-5,7,9,11,13-pentaphosphaheptadecane-1,17-diyl ester, [2S-[2R*[S*(R*)],16R*[S*(R*)]]]-(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

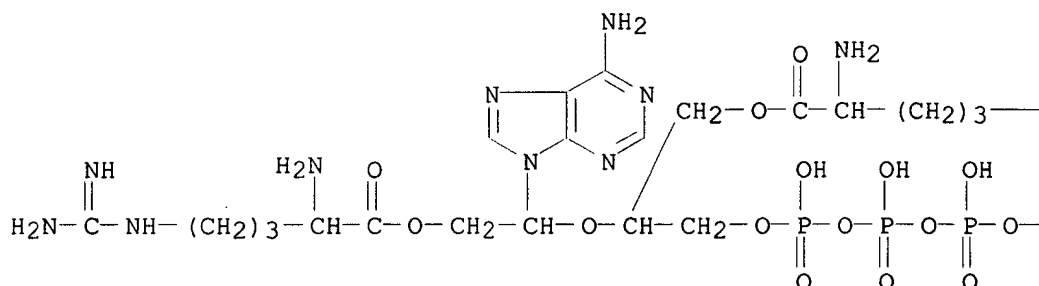
CN L-Arginine, 2,16-bis[2-[[2-amino-5-[(aminoiminomethyl)amino]-1-oxopentyl]oxy]-1-(6-amino-9H-purin-9-yl)ethoxy]-5,7,9,11,13-pentahydroxy-4,6,8,10,12,14-hexaoxa-5,7,9,11,13-pentaphosphaheptadecane-1,17-diyl ester, P,P',P'',P''',P''''-pentaoxide, [2S-[2R*[S*(R*)],16R*[S*(R*)]]]-(9CI)

MF C44 H81 N26 O26 P5

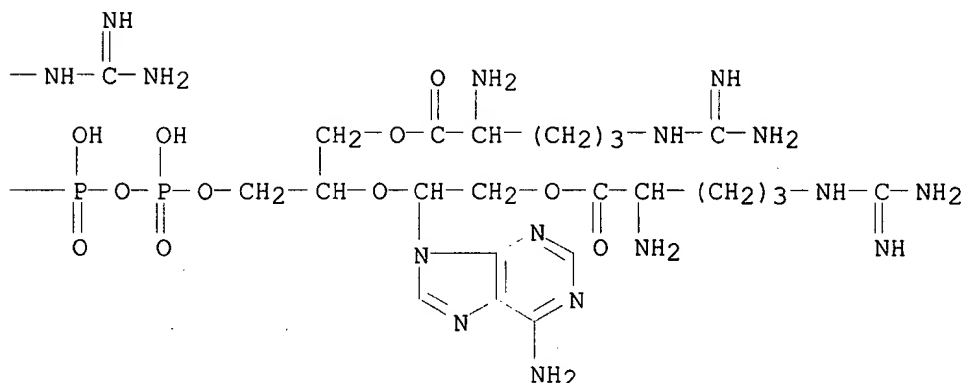
SR CA

LC STN Files: CA, CAPLUS

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PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 106:151984 Biochemistry of terminal deoxynucleotidyltransferase (TdT): characterization and mechanism of inhibition of TdT by P1,P5-bis(5'-adenosyl) pentaphosphate. Pandey, Virendranath; Modak, Mukund J. (New Jersey Med. Sch., Univ. Med. Dent. New Jersey, Newark, NJ, 07103, USA). Biochemistry, 26(7), 2033-8 (English) 1987. CODEN: BICHAW. ISSN: 0006-2960.

AB The catalysis of DNA synthesis of calf thymus TdT was strongly inhibited in the presence of Ap5A, whereas replicative DNA polymerases from

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mammalian, bacterial, and oncornaviral sources were totally insensitive to Ap5A addn. The Ap5A-mediated inhibition of TdT appeared to occur via its interaction at both the substrate-binding and primer-binding domains as judged by (a) classical competitive inhibition plots with respect to both substrate deoxynucleoside triphosphate (dNTP) and DNA primer and (b) inhibition of UV light-mediated crosslinking of substrate dNTP and oligomeric DNA primer to their resp. binding sites. Further kinetic analyses of Ap5A inhibition revealed that the dissocn. const. of the Ap5A-enzyme complex, with either substrate binding or primer binding domain participating in the complex formation, was .apprx.6-fold higher ($K_i = 1.5 \text{ } \mu\text{M}$) compared to the dissocn. const. ($K_i = 0.25 \text{ } \mu\text{M}$) of the Ap5A-TdT complex when both domains were available for binding. In order to study the binding stoichiometry of Ap5A to TdT, an oxidized deriv. of Ap5A, which exhibited identical inhibitory properties as its parent compd., was employed. The oxidn. product of Ap5A, presumably a tetraaldehyde deriv., bound irreversibly to TdT when inhibitor-enzyme complex was subjected to borohydride redn. The presence of aldehyde groups in the oxidized Ap5A appeared essential for inhibitory activity since its redn. to alc. via borohydride redn. or its linkage to free amino acids prior to use as an inhibitor rendered it completely ineffective. With use of a tritiated oxidn. product of Ap5A, a binding stoichiometry of 1 mol of Ap5A to 1 mol of TdT was obsd. Thus, a single Ap5A mol. appears to span across both the substrate and primer binding site domains in TdT.

L13 ANSWER 103 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 107148-03-8 REGISTRY

CN Glycine, 2,16-bis[2-[(aminoacetyl)oxy]-1-(6-amino-9H-purin-9-yl)ethoxy]-5,7,9,11,13-pentahydroxy-4,6,8,10,12,14-hexaoxa-5,7,9,11,13-pentaphosphaheptadecane-1,17-diyl ester, [2S-[2R*(S*),16R*(S*)]]-(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

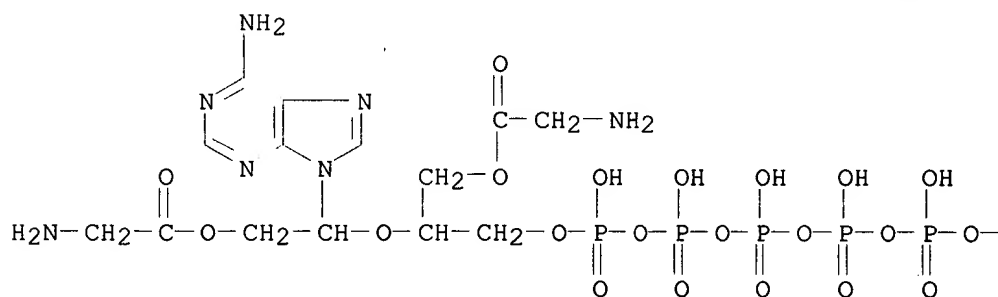
CN Glycine, 2,16-bis[2-[(aminoacetyl)oxy]-1-(6-amino-9H-purin-9-yl)ethoxy]-5,7,9,11,13-pentahydroxy-4,6,8,10,12,14-hexaoxa-5,7,9,11,13-pentaphosphaheptadecane-1,17-diyl ester, P,P',P'',P''',P''''-pentaoxide, [2S-[2R*(S*),16R*(S*)]]-

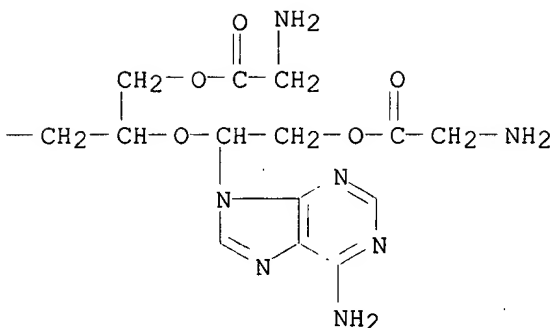
MF C28 H45 N14 O26 P5

SR CA

LC STN Files: CA, CAPLUS

PAGE 1-A





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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 106:151984 Biochemistry of terminal deoxynucleotidyltransferase (TdT): characterization and mechanism of inhibition of TdT by P1,P5-bis(5'-adenosyl) pentaphosphate. Pandey, Virendranath; Modak, Mukund J. (New Jersey Med. Sch., Univ. Med. Dent. New Jersey, Newark, NJ, 07103, USA). Biochemistry, 26(7), 2033-8 (English) 1987. CODEN: BICHAW. ISSN: 0006-2960.

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L13 ANSWER 104 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 107148-02-7 REGISTRY

CN Pentaphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] P''''-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-8-t)-

2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

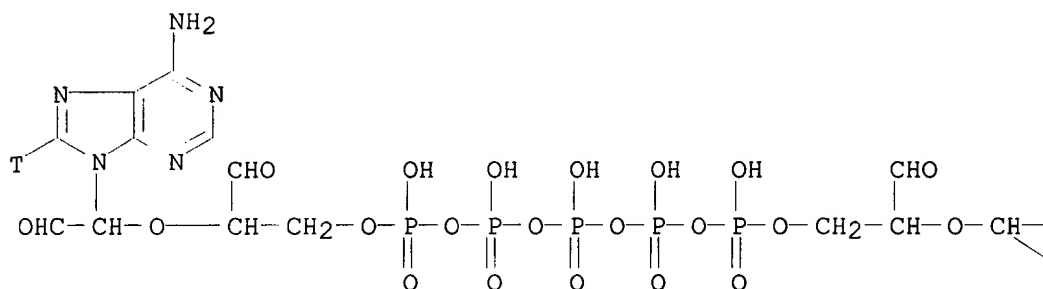
CN Pentaphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] P''''-[2-[1-(6-amino-9H-purin-9-yl-8-t)-2-oxoethoxy]-3-oxopropyl] ester, [2R-[1[R*(R*)],2R*(R*)]]-

MF C20 H24 N10 O22 P5 T

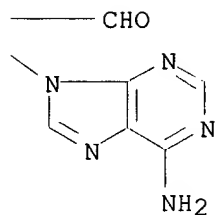
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LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 106:151984 Biochemistry of terminal deoxynucleotidyltransferase (TdT): characterization and mechanism of inhibition of TdT by P1,P5-bis(5'-adenosyl) pentaphosphate. Pandey, Virendranath; Modak, Mukund J. (New Jersey Med. Sch., Univ. Med. Dent. New Jersey, Newark, NJ, 07103, USA). Biochemistry, 26(7), 2033-8 (English) 1987. CODEN: BICHAW. ISSN: 0006-2960.

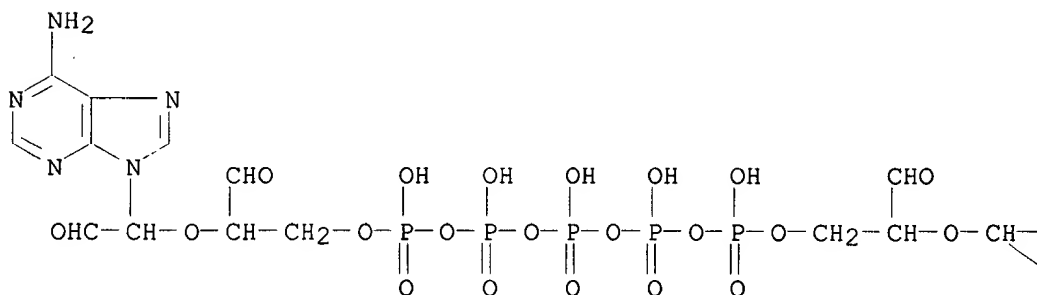
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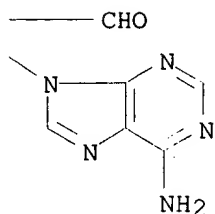
Searched by: Mary Hale 308-4258 CM-1 12D16

oligomeric DNA primer to their resp. binding sites. Further kinetic analyses of Ap5A inhibition revealed that the dissocn. const. of the Ap5A-enzyme complex, with either substrate binding or primer binding domain participating in the complex formation, was .apprx.6-fold higher ($K_i = 1.5 \mu\text{M}$) compared to the dissocn. const. ($K_i = 0.25 \mu\text{M}$) of the Ap5A-TdT complex when both domains were available for binding. In order to study the binding stoichiometry of Ap5A to TdT, an oxidized deriv. of Ap5A, which exhibited identical inhibitory properties as its parent compd., was employed. The oxidn. product of Ap5A, presumably a tetraaldehyde deriv., bound irreversibly to TdT when inhibitor-enzyme complex was subjected to borohydride redn. The presence of aldehyde groups in the oxidized Ap5A appeared essential for inhibitory activity since its redn. to alc. via borohydride redn. or its linkage to free amino acids prior to use as an inhibitor rendered it completely ineffective. With use of a tritiated oxidn. product of Ap5A, a binding stoichiometry of 1 mol of Ap5A to 1 mol of TdT was obsd. Thus, a single Ap5A mol. appears to span across both the substrate and primer binding site domains in TdT.

L13 ANSWER 105 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 107148-01-6 REGISTRY
 CN Pentaphosphoric acid, P,P''''-bis[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [2R-[1[R*(R*)],2R*(R*)]]- (9CI) (CA INDEX NAME)
 MF C20 H25 N10 O22 P5
 CI COM
 SR CA
 LC STN Files: CA, CAPLUS

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 106:151984 Biochemistry of terminal deoxynucleotidyltransferase (TdT): characterization and mechanism of inhibition of TdT by P1,P5-bis(5'-adenosyl) pentaphosphate. Pandey, Virendranath; Modak, Mukund J. (New Jersey Med. Sch., Univ. Med. Dent. New Jersey, Newark, NJ, 07103, USA). Biochemistry, 26(7), 2033-8 (English) 1987. CODEN: BICHAW. ISSN: 0006-2960.

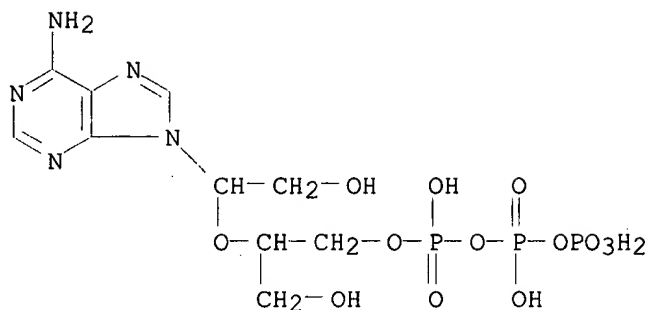
AB The catalysis of DNA synthesis of calf thymus TdT was strongly inhibited in the presence of Ap5A, whereas replicative DNA polymerases from mammalian, bacterial, and oncornaviral sources were totally insensitive to Ap5A addn. The Ap5A-mediated inhibition of TdT appeared to occur via its interaction at both the substrate-binding and primer-binding domains as judged by (a) classical competitive inhibition plots with respect to both substrate deoxynucleoside triphosphate (dNTP) and DNA primer and (b) inhibition of UV light-mediated crosslinking of substrate dNTP and oligomeric DNA primer to their resp. binding sites. Further kinetic analyses of Ap5A inhibition revealed that the dissocn. const. of the Ap5A-enzyme complex, with either substrate binding or primer binding domain participating in the complex formation, was .apprx.6-fold higher ($K_i = 1.5 \mu\text{M}$) compared to the dissocn. const. ($K_i = 0.25 \mu\text{M}$) of the Ap5A-TdT complex when both domains were available for binding. In order to study the binding stoichiometry of Ap5A to TdT, an oxidized deriv. of Ap5A, which exhibited identical inhibitory properties as its parent compd., was employed. The oxidn. product of Ap5A, presumably a tetraaldehyde deriv., bound irreversibly to TdT when inhibitor-enzyme complex was subjected to borohydride redn. The presence of aldehyde groups in the oxidized Ap5A appeared essential for inhibitory activity since its redn. to alc. via borohydride redn. or its linkage to free amino acids prior to use as an inhibitor rendered it completely ineffective. With use of a tritiated oxidn. product of Ap5A, a binding stoichiometry of 1 mol of Ap5A to 1 mol of TdT was obsd. Thus, a single Ap5A mol. appears to span across both the substrate and primer binding site domains in TdT.

L13 ANSWER 106 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 102185-15-9 REGISTRY

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, trisodium salt (9CI) (CA INDEX NAME)

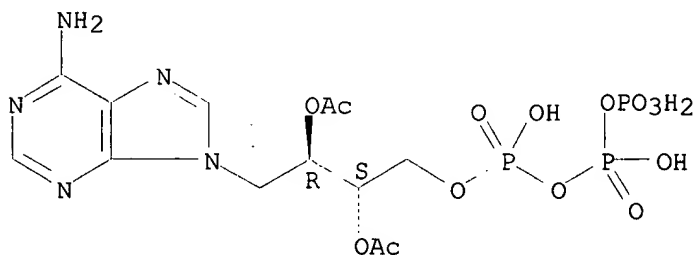
MF C10 H18 N5 O13 P3 . 3 Na
 SR CAS Registry Services
 LC STN Files: CHEMCATS
 CRN (120083-53-6)



● 3 Na

L13 ANSWER 107 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 99689-06-2 REGISTRY
 CN Erythritol, 1-(6-amino-9H-purin-9-yl)-1-deoxy-, 2,3-diacetate
 4-triphosphate, tetralithium salt (7CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C13 H20 N5 O14 P3 . 4 Li
 SR CAOLD
 LC STN Files: CAOLD
 CRN (108267-43-2)

Absolute stereochemistry.



● 4 Li

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L13 ANSWER 108 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 98815-99-7 REGISTRY
 CN Phosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] mono[2,10-bis(6-amino-9H-purin-9-yl)-7,13-dihydroxy-4,12-bis(hydroxymethyl)-7-oxido-3,6,8,11-tetraoxa-7-phosphatridec-1-yl] ester, stereoisomer (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Phosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] mono[2,10-bis(6-amino-9H-purin-9-yl)-7,13-dihydroxy-4,12-

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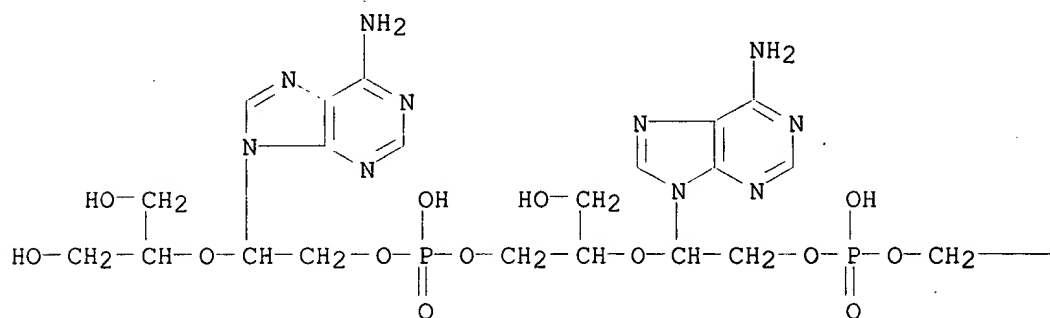
bis(hydroxymethyl)-3,6,8,11-tetraoxa-7-phosphatridec-1-yl] ester, P-oxide, stereoisomer

MF C30 H43 N15 O16 P2

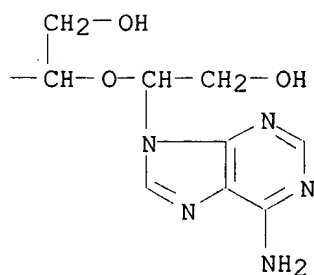
SR CA

LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)

4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 110:68997 A route to 2',5'-oligoadenylates with increased stability towards phosphodiesterases. Itkes, A. V.; Karpeiskii, M. Ya.; Kartasheva, O. N.; Mikhailov, S. N.; Moiseev, G. P.; Pfleiderer, W.; Charubala, R.; Yakovlev, G. I. (Inst. Mol. Biol., Moscow, 117984, USSR). Mol. Biol. (Moscow), 22(5), 1393-8 (Russian) 1988. CODEN: MOBIBO. ISSN: 0026-8984.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16

AB Oligoadenylates with a 2',5'-phosphate bond are mediators of antiviral action of interferons but are unstable to phosphodiesterase. Analogs of these compds. [I, R = OH, R1 = O(CH₂)_n-adenine, O(CH₂)₂OCH₂-adenine, OCH₂CH(CH₂OH)OCH(CH₂OH)-adenine, etc.] were prepd. by the std. methods starting from II and reaction with acyclic analogs of nucleosides in the presence of 2,4,6-triisopropylbenzenesulfonyl chloride and N-methylimidazole, and deblocking. These analogs were treated with NIH3T3 cell lysates, mice liver homogenates and snake venom phosphodiesterase. The compds. were more stable than the natural I (R = OH or R = H; R1 = 5'-adenosyl).

REFERENCE 2: 110:53529 A route to 2',5'-oligoadenylates with increased stability towards phosphodiesterases. Itkes, A. V.; Karpeiskii, M. Ya.; Kartasheva, O. N.; Mikhailov, S. N.; Moiseev, G. P.; Pfleiderer, W.; Charubala, R.; Yakovlev, G. I. (Inst. Mol. Biol., Moscow, 117984, USSR). FEBS Lett., 236(2), 325-8 (English) 1988. CODEN: FEBLAL. ISSN: 0014-5793.

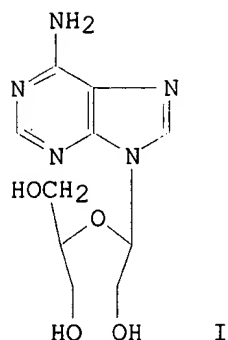
AB The rates of enzymic hydrolysis of 2',5'-oligoadenylates and their synthetic analogs were measured. These compds. were treated with either NIH 3T3 cell lysates, mouse liver homogenates, or snake venom phosphodiesterase. All analogs with 3'-terminal acyclic nucleoside residues demonstrated greater stability compared with the natural compd., adenylyl(2'-5')adenylyl(2'-5')adenosine.

REFERENCE 3: 105:151228 Biological activity of new 2-5A analogs. Pauwels, R.; De Clercq, E.; Balzarini, J.; Sawai, H.; Imbach, J. L.; Gosselin, G.; Huss, S.; Reese, C. B.; Serafinowska, H.; et al. (Rega Inst. Med. Res., Univ. Leuven, Louvain, B-3000, Belg.). Chem. Scr., 26(1), 141-5 (English) 1986. CODEN: CSRPB9. ISSN: 0004-2056.

AB Of a series of newly synthesized 2'-5' oligoadenylate (2-5A) analogs (with modifications in the ribose-phosphate backbone), several compds. proved effective as antimitogenic and antiproliferative agents. The antimitogenic activity was based upon the inhibition of DNA and protein synthesis in synchronized (serum-starved) Balb/c 3T3 cells, whereas the antiproliferative activity was detd. by monitoring the inhibition of murine leukemia L1210 cell growth. The antiproliferative effects of 2-5 A analogs correlated closely with their inhibitory effects on DNA and protein synthesis. When considered on a monomer equiv. basis, the mixed adenosine-cordycepin (1:2) cotrimer was more active than the cordycepin monomer, the phosphoramidate-linked adenosine trimer was less active than the aminoadenosine monomer, whereas the aristeromycin trimer, the xyloadenosine tri- and tetramers and the mixed adenosine-xyloadenosine (1:2, 2:1, 2:2, 1:3) tri- or tetramers were about equally active as either the aristeromycin or xyloadenosine monomer. It is likely that the latter 2-5A analogs owe their biol. activity to degrdn. to their monomer units.

REFERENCE 4: 103:178558 Synthesis of a new class of acyclic 2',5'- and 3',5'-oligonucleotide analogs based on 9-[1,5-dihydroxy-4-(S)-hydroxymethyl-3-oxapent-2(R)-yl]adenine. Mikhailov, S. N.; Pfleiderer, Wolfgang (Inst. Mol. Biol., Moscow, B-334, USSR). Tetrahedron Lett., 26(17), 2059-62 (English) 1985. CODEN: TELEAY. ISSN: 0040-4039.

GI



AB The acyclic analogs of 2',5'- and 3',5'-oligoadenylates possessing all functional groups of the natural compds. were prepd. on the basis of "oxidized-reduced" adenosine (I).

L13 ANSWER 109 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 98815-98-6 REGISTRY

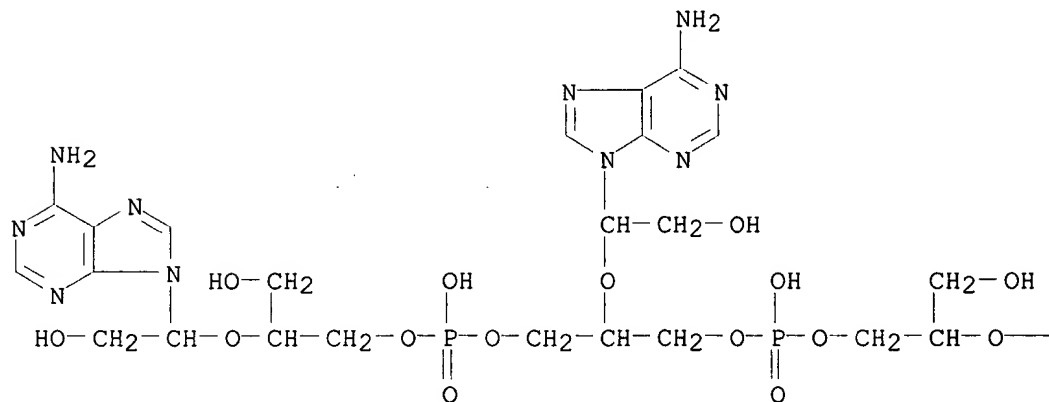
CN Phosphoric acid, P,P'-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-1,3-propanediyl] P,P'-bis[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]propyl] ester, stereoisomer (9CI) (CA INDEX NAME)

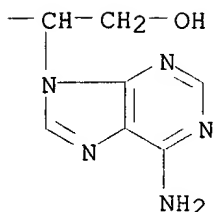
MF C30 H43 N15 O16 P2

SR CA

LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)

PAGE 1-A





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GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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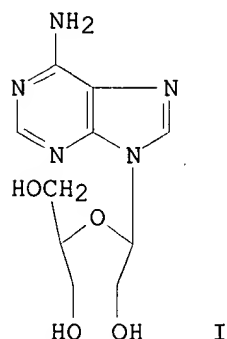
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REFERENCE 3: 105:151228 Biological activity of new 2-5A analogs. Pauwels, R.; De Clercq, E.; Balzarini, J.; Sawai, H.; Imbach, J. L.; Gosselin, G.; Huss, S.; Reese, C. B.; Serafinowska, H.; et al. (Rega Inst. Med. Res., Univ. Leuven, Louvain, B-3000, Belg.). Chem. Scr., 26(1), 141-5 (English) 1986. CODEN: CSRPB9. ISSN: 0004-2056.

AB Of a series of newly synthesized 2'-5' oligoadenylate (2-5A) analogs (with modifications in the ribose-phosphate backbone), several compds. proved effective as antimitogenic and antiproliferative agents. The antimitogenic activity was based upon the inhibition of DNA and protein synthesis in synchronized (serum-starved) Balb/c 3T3 cells, whereas the antiproliferative activity was detd. by monitoring the inhibition of murine leukemia L1210 cell growth. The antiproliferative effects of 2-5 A analogs correlated closely with their inhibitory effects on DNA and protein synthesis. When considered on a monomer equiv. basis, the mixed adenosine-cordycepin (1:2) cotrimer was more active than the cordycepin monomer, the phosphoramidate-linked adenosine trimer was less active than the aminoadenosine monomer, whereas the aristeromycin trimer, the xyloadenosine tri- and tetramers and the mixed adenosine-xyloadenosine (1:2, 2:1, 2:2, 1:3) tri- or tetramers were about equally active as either the aristeromycin or xyloadenosine monomer. It is likely that the latter 2-5A analogs owe their biol. activity to degradn. to their monomer units.

REFERENCE 4: 103:178558 Synthesis of a new class of acyclic 2',5'- and 3',5'-oligonucleotide analogs based on 9-[1,5-dihydroxy-4-(S)-hydroxymethyl-3-oxapent-2(R)-yl]adenine. Mikhailov, S. N.; Pfleiderer, Wolfgang (Inst. Mol. Biol., Moscow, B-334, USSR). Tetrahedron Lett., 26(17), 2059-62 (English) 1985. CODEN: TELEAY. ISSN: 0040-4039.

GI



AB The acyclic analogs of 2',5'- and 3',5'-oligoadenylates possessing all functional groups of the natural compds. were prepd. on the basis of "oxidized-reduced" adenosine (I).

L13 ANSWER 110 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 98815-97-5 REGISTRY

CN Phosphoric acid, 2-[1-[6-(benzoylamino)-9H-purin-9-yl]-2-(benzoyloxy)ethoxy]-3-(benzoyloxy)propyl 2,10-bis[6-(benzoylamino)-9H-purin-9-yl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-12-(hydroxymethyl)-7-[2-(4-nitrophenyl)ethyl]-15,15,16,16-tetramethyl-7-oxido-3,6,8,11,14-pentaoxa-7-phospha-15-silaheptadec-1-yl 2-(4-nitrophenyl)ethyl

Searched by: Mary Hale 308-4258 CM-1 12D16

ester, stereoisomer (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

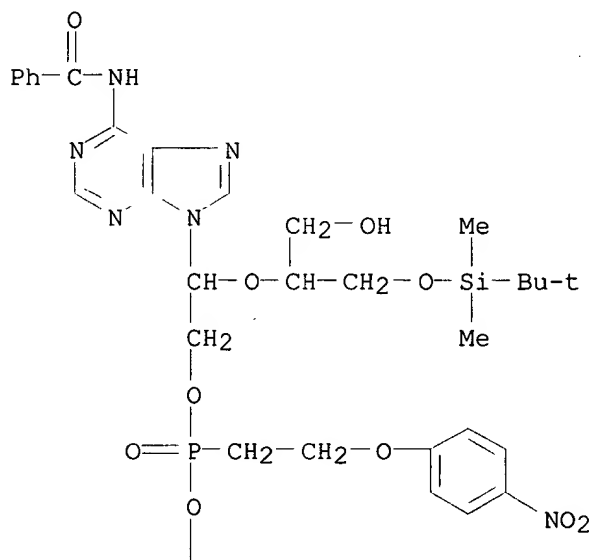
CN Phosphoric acid, 2-[1-[6-(benzoylamino)-9H-purin-9-yl]-2-(benzoyloxy)ethoxy]-3-(benzoyloxy)propyl 2,10-bis[6-(benzoylamino)-9H-purin-9-yl]-4-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-12-(hydroxymethyl)-7-[2-(4-nitrophenyl)ethyl]-15,15,16,16-tetramethyl-3,6,8,11,14-pentaoxa-7-phospha-15-silaheptadec-1-yl 2-(4-nitrophenyl)ethyl ester, P-oxide, stereoisomer

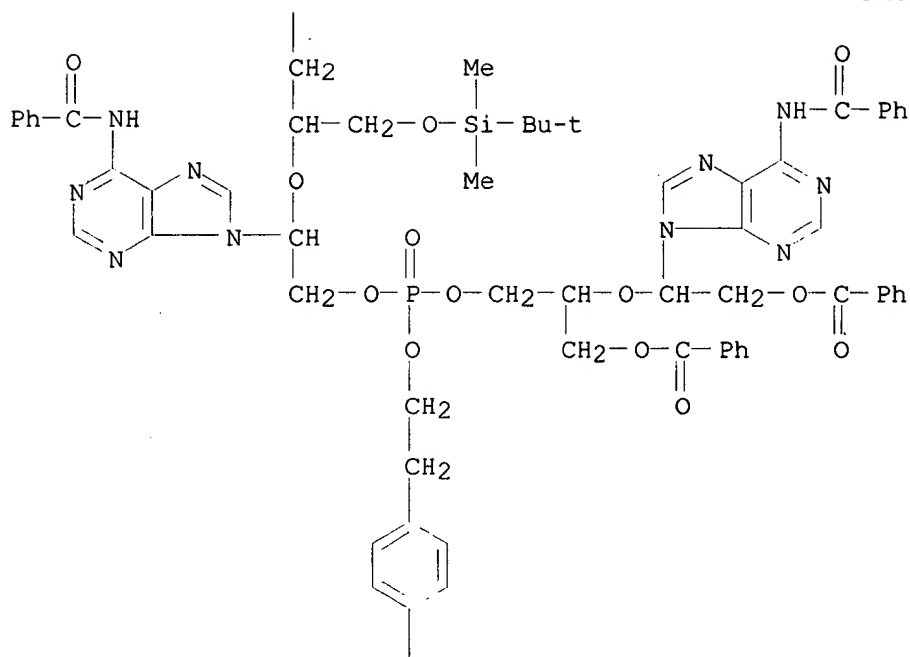
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SR CA

LC STN Files: CA, CAPLUS, CASREACT

PAGE 1-A





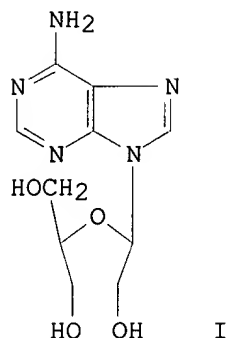
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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 103:178558 Synthesis of a new class of acyclic 2',5'- and 3',5'-oligonucleotide analogs based on 9-[1,5-dihydroxy-4-(S)-hydroxymethyl-3-oxapent-2(R)-yl]adenine. Mikhailov, S. N.; Pflleiderer, Wolfgang (Inst. Mol. Biol., Moscow, B-334, USSR). Tetrahedron Lett., 26(17), 2059-62 (English) 1985. CODEN: TELEAY. ISSN: 0040-4039.

GI



AB The acyclic analogs of 2',5'- and 3',5'-oligoadenylates possessing all functional groups of the natural compds. were prepd. on the basis of "oxidized-reduced" adenosine (I).

L13 ANSWER 111 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 98815-96-4 REGISTRY

CN Phosphoric acid, 10-[6-(benzoylamino)-9H-purin-9-yl]-2-[1-[6-(benzoylamino)-9H-purin-9-yl]-2-[[1,1-dimethylethyl]dimethylsilyl]oxy]ethoxy]-8-[(benzoyloxy)methyl]-5-[2-(4-nitrophenyl)ethoxy]-5-oxido-13-oxo-13-phenyl-4,6,9,12-tetraoxa-5-phosphatridec-1-yl 2-[1-[6-(benzoylamino)-9H-purin-9-yl]-3-[[1,1-dimethylethyl]dimethylsilyl]oxy]ethoxy]-3-hydroxypropyl 2-(4-nitrophenyl)ethyl ester, stereoisomer (9CI) (CA INDEX NAME)

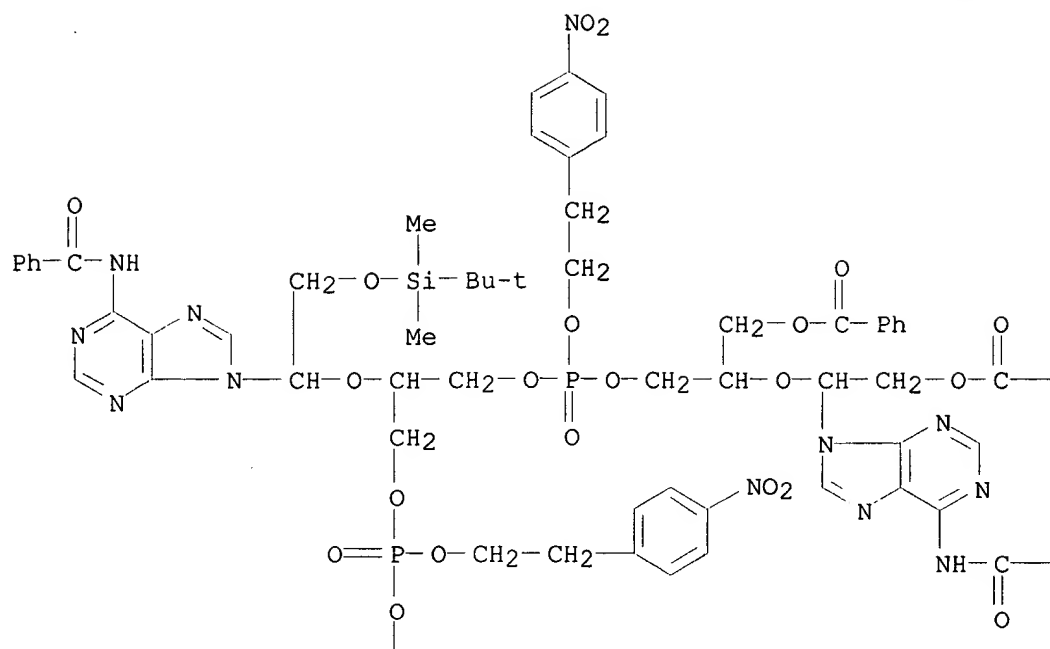
OTHER CA INDEX NAMES:

CN Phosphoric acid, 10-[6-(benzoylamino)-9H-purin-9-yl]-2-[1-[6-(benzoylamino)-9H-purin-9-yl]-2-[[1,1-dimethylethyl]dimethylsilyl]oxy]ethoxy]-8-[(benzoyloxy)methyl]-5-[2-(4-nitrophenyl)ethoxy]-13-oxo-13-phenyl-4,6,9,12-tetraoxa-5-phosphatridec-1-yl 2-[1-[6-(benzoylamino)-9H-purin-9-yl]-3-[[1,1-dimethylethyl]dimethylsilyl]oxy]ethoxy]-3-hydroxypropyl 2-(4-nitrophenyl)ethyl ester, P-oxide, stereoisomer

MF C93 H105 N17 O25 P2 Si2

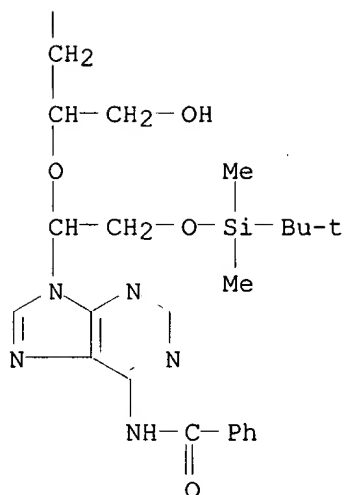
SR CA

LC STN Files: CA, CAPLUS, CASREACT



— Ph

— Ph

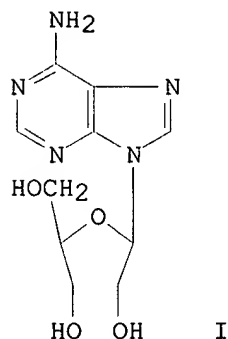


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 103:178558 Synthesis of a new class of acyclic 2',5'- and 3',5'-oligonucleotide analogs based on 9-[1,5-dihydroxy-4-(S)-hydroxymethyl-3-oxapent-2(R)-yl]adenine. Mikhailov, S. N.; Pfleiderer, Wolfgang (Inst. Mol. Biol., Moscow, B-334, USSR). Tetrahedron Lett., 26(17), 2059-62 (English) 1985. CODEN: TELEAY. ISSN: 0040-4039.

GI

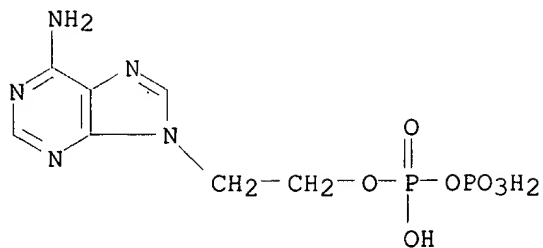


I

AB The acyclic analogs of 2',5'- and 3',5'-oligoadenylates possessing all functional groups of the natural compds. were prepd. on the basis of "oxidized-reduced" adenosine (I).

L13 ANSWER 112 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 98335-84-3 REGISTRY
CN 9H-Purine-9-ethanol, 6-amino-, diphosphate (6CI) (CA INDEX NAME)
FS 3D CONCORD
MF C7 H11 N5 O7 P2
SR CAOLD
LC STN Files: CAOLD

Searched by: Mary Hale 308-4258 CM-1 12D16

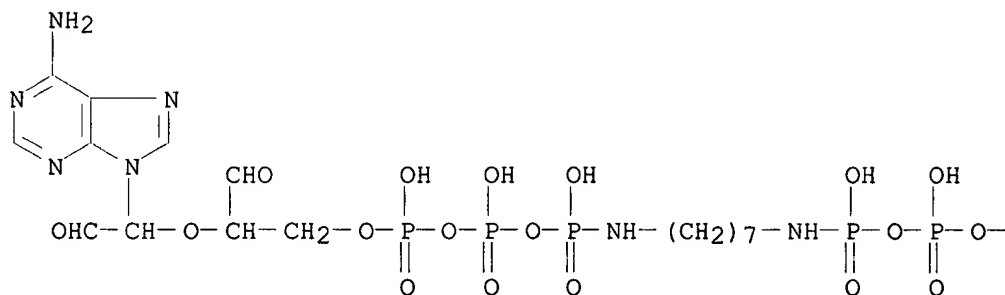


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

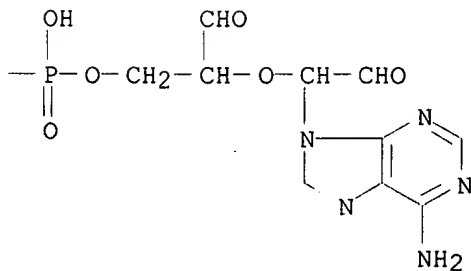
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L13 ANSWER 113 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 97287-72-4 REGISTRY
 CN P-Amidotriphosphoric acid, N,N'-1,7-heptanediylbis-, P'',P''''-bis[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, stereoisomer (9CI) (CA INDEX NAME)
 MF C27 H42 N12 O24 P6
 LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

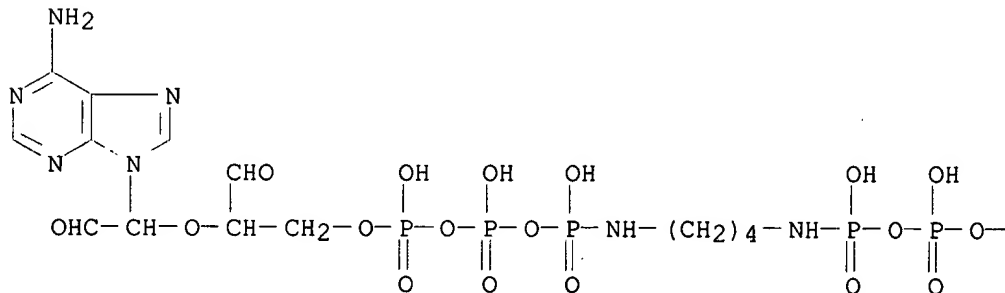
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

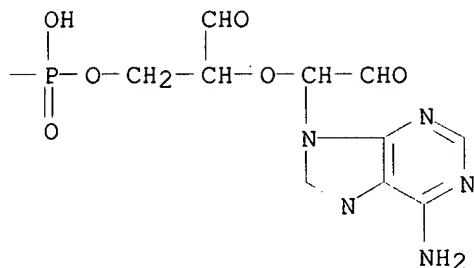
REFERENCE 1: 103:50262 Interaction of some nucleotide-dependent enzymes with bifunctional analogs of ATP: derivatives of polymethylenediamines. Nevinskii, G. A.; Vtorushina, I. A.; Bulychev, N. V.; Kovaleva, G. K.; Lavrik, O. I. (Novosibirsk Inst. Org. Chem., Novosibirsk, USSR). Mol. Biol. (Moscow), 19(2), 467-78 (Russian) 1985. CODEN: MOBIBO. ISSN: 0026-8984.

AB The interaction of bifunctional ATP derivs., Appp5'[NH(CH₂)_nNH]ppp5'A (n = 0 or 2-8) with tyrosyl-, valyl-, lysyl-, and tryptophanyl-tRNA synthetases and creatine kinase was investigated. ATP derivs. don't inhibit the tRNA aminoacylation catalyzed by tyrosyl-tRNA synthetase. These derivs. behave as mixed-type inhibitors with respect to ATP in the case of valyl- and lysyl-tRNA synthetases. In the case of the other enzymes, all analogs of ATP manifest competitive inhibition towards ATP. The affinity of all ATP derivs. to tryptophanyl-tRNA synthetase does not differ significantly (K_i = 0.2-0.6 mM). The K_i values for these derivs. in the case of creatine kinase are also very similar with the exception of A5'pppNH(CH₂)₃NHppp5'A. The K_i value for this deriv. is 1 order of magnitude lower than for the other ones. The affinity reagents prep'd. by IO₄⁻ oxidn. of bifunctional ATP analog derivs. of di-, tetra-, and heptamethylenediamine modify nonidentical subunits of creatine kinase with different velocities, but modification of the M and M' subunits proceeds independently. An analog of trimethylenediamine interacts simultaneously with 2 centers of the dimeric form of kinase, forming nonequivalent complexes. The covalent attachment of the reagent to 1 subunit of creatine kinase does not prohibit complex formation and covalent binding of bifunctional ATP analogs to the other subunit of the dimer, but results in a 10-fold decrease in affinity of the ATP deriv. for the nonmodified center of the enzyme. These data permit an evaluation of the distance between the ATP-binding sites of creatine kinase in its dimeric form as .apprx.5-6 .ANG.. Such a distance between active sites may be the reason for the higher activity of the M and M' creatine kinase subunits taken sep. as compared to the enzyme dimeric form.

L13 ANSWER 114 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 97287-71-3 REGISTRY
CN P-Amidotriphosphoric acid, N,N'-1,4-butanediylbis-, P'',P''''-bis[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, stereoisomer (9CI)
(CA INDEX NAME)
MF C24 H36 N12 O24 P6
LC STN Files: CA, CAPLUS

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

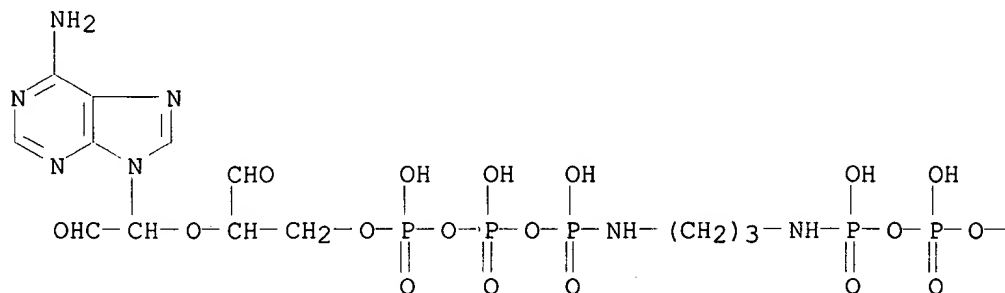
REFERENCE 1: 103:50262 Interaction of some nucleotide-dependent enzymes with bifunctional analogs of ATP: derivatives of polymethylenediamines.

Nevinskii, G. A.; Vtorushina, I. A.; Bulychev, N. V.; Kovaleva, G. K.; Lavrik, O. I. (Novosibirsk Inst. Org. Chem., Novosibirsk, USSR). Mol. Biol. (Moscow), 19(2), 467-78 (Russian) 1985. CODEN: MOBIBO. ISSN: 0026-8984.

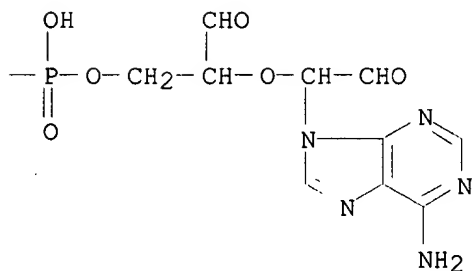
AB The interaction of bifunctional ATP derivs., Appp5'[NH(CH2)*n*NH]ppp5'A (*n* = 0 or 2-8) with tyrosyl-, valyl-, lysyl-, and tryptophanyl-tRNA synthetases and creatine kinase was investigated. ATP derivs. don't inhibit the tRNA aminoacylation catalyzed by tyrosyl-tRNA synthetase. These derivs. behave as mixed-type inhibitors with respect to ATP in the case of valyl- and lysyl-tRNA synthetases. In the case of the other enzymes, all analogs of ATP manifest competitive inhibition towards ATP. The affinity of all ATP derivs. to tryptophanyl-tRNA synthetase does not differ significantly (*K_i* = 0.2-0.6 mM). The *K_i* values for these derivs. in the case of creatine kinase are also very similar with the exception of A5'pppNH(CH2)3NHppp5'A. The *K_i* value for this deriv. is 1 order of magnitude lower than for the other ones. The affinity reagents prep'd. by IO4- oxidn. of bifunctional ATP analog derivs. of di-, tetra-, and heptamethylenediamine modify nonidentical subunits of creatine kinase with different velocities, but modification of the M and M' subunits proceeds independently. An analog of trimethylenediamine interacts simultaneously with 2 centers of the dimeric form of kinase, forming nonequivalent complexes. The covalent attachment of the reagent to 1 subunit of creatine kinase does not prohibit complex formation and covalent binding of bifunctional ATP analogs to the other subunit of the dimer, but results in a 10-fold decrease in affinity of the ATP deriv. for the nonmodified center of the enzyme. These data permit an evaluation of the distance between the ATP-binding sites of creatine kinase in its dimeric form as .apprx.5-6 .ANG.. Such a distance between active sites may be the reason for the higher activity of the M and M' creatine kinase subunits taken sep. as compared to the enzyme dimeric form.

L13 ANSWER 115 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 97287-70-2 REGISTRY
 CN P-Amidotriphosphoric acid, N,N'-1,3-propanediylbis-, P'',P''''-bis[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, stereoisomer (9CI) (CA INDEX NAME)
 MF C23 H34 N12 O24 P6
 LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

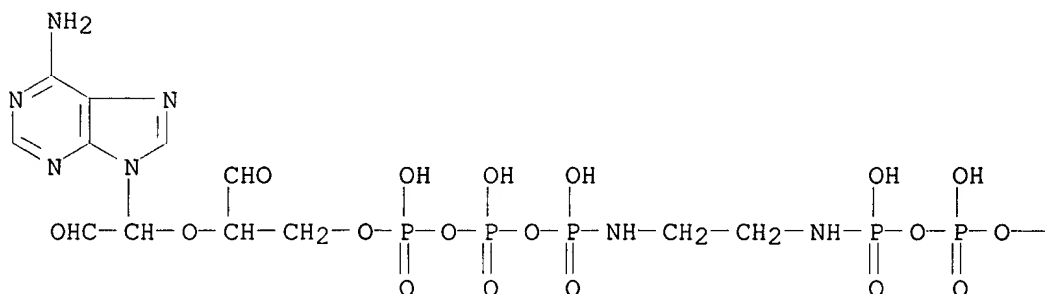
- REFERENCE 1: 103:50262 Interaction of some nucleotide-dependent enzymes with bifunctional analogs of ATP: derivatives of polymethylenediamines. Nevinskii, G. A.; Vtorushina, I. A.; Bulychiev, N. V.; Kovaleva, G. K.; Lavrik, O. I. (Novosibirsk Inst. Org. Chem., Novosibirsk, USSR). Mol. Biol. (Moscow), 19(2), 467-78 (Russian) 1985. CODEN: MOBIBO. ISSN: 0026-8984.
- AB The interaction of bifunctional ATP derivs., Appp5'[NH(CH2)nNH]ppp5'A (n = 0 or 2-8) with tyrosyl-, valyl-, lysyl-, and tryptophanyl-tRNA synthetases and creatine kinase was investigated. ATP derivs. don't inhibit the tRNA aminoacylation catalyzed by tyrosyl-tRNA synthetase. These derivs. behave as mixed-type inhibitors with respect to ATP in the case of valyl- and

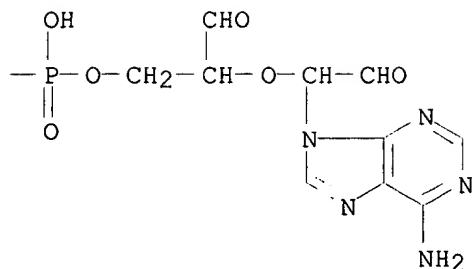
Searched by: Mary Hale 308-4258 CM-1 12D16

lysyl-tRNA synthetases. In the case of the other enzymes, all analogs of ATP manifest competitive inhibition towards ATP. The affinity of all ATP derivs. to tryptophanyl-tRNA synthetase does not differ significantly ($K_i = 0.2-0.6$ mM). The K_i values for these derivs. in the case of creatine kinase are also very similar with the exception of A5'pppNH(CH₂)₃NHppp5'A. The K_i value for this deriv. is 1 order of magnitude lower than for the other ones. The affinity reagents prep'd. by IO₄⁻ oxidn. of bifunctional ATP analog derivs. of di-, tetra-, and heptamethylenediamine modify nonidentical subunits of creatine kinase with different velocities, but modification of the M and M' subunits proceeds independently. An analog of trimethylenediamine interacts simultaneously with 2 centers of the dimeric form of kinase, forming nonequivalent complexes. The covalent attachment of the reagent to 1 subunit of creatine kinase does not prohibit complex formation and covalent binding of bifunctional ATP analogs to the other subunit of the dimer, but results in a 10-fold decrease in affinity of the ATP deriv. for the nonmodified center of the enzyme. These data permit an evaluation of the distance between the ATP-binding sites of creatine kinase in its dimeric form as .apprx.5-6 .ANG.. Such a distance between active sites may be the reason for the higher activity of the M and M' creatine kinase subunits taken sep. as compared to the enzyme dimeric form.

L13 ANSWER 116 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 97287-69-9 REGISTRY
 CN P-Amidotriphosphoric acid, N,N'-1,2-ethanediylbis-, P'',P''''-bis[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, stereoisomer (9CI)
 (CA INDEX NAME)
 MF C22 H32 N12 O24 P6
 LC STN Files: CA, CAPLUS

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 103:50262 Interaction of some nucleotide-dependent enzymes with bifunctional analogs of ATP: derivatives of polymethylenediamines. Nevinskii, G. A.; Vtorushina, I. A.; Bulychiev, N. V.; Kovaleva, G. K.; Lavrik, O. I. (Novosibirsk Inst. Org. Chem., Novosibirsk, USSR). Mol. Biol. (Moscow), 19(2), 467-78 (Russian) 1985. CODEN: MOBIBO. ISSN: 0026-8984.

AB The interaction of bifunctional ATP derivs., Appp5'[NH(CH2)nNH]ppp5'A (n = 0 or 2-8) with tyrosyl-, valyl-, lysyl-, and tryptophanyl-tRNA synthetases and creatine kinase was investigated. ATP derivs. don't inhibit the tRNA aminoacylation catalyzed by tyrosyl-tRNA synthetase. These derivs. behave as mixed-type inhibitors with respect to ATP in the case of valyl- and lysyl-tRNA synthetases. In the case of the other enzymes, all analogs of ATP manifest competitive inhibition towards ATP. The affinity of all ATP derivs. to tryptophanyl-tRNA synthetase does not differ significantly ($K_i = 0.2-0.6$ mM). The K_i values for these derivs. in the case of creatine kinase are also very similar with the exception of A5'pppNH(CH2)3NHppp5'A. The K_i value for this deriv. is 1 order of magnitude lower than for the other ones. The affinity reagents prepd. by IO4- oxidn. of bifunctional ATP analog derivs. of di-, tetra-, and heptamethylenediamine modify nonidentical subunits of creatine kinase with different velocities, but modification of the M and M' subunits proceeds independently. An analog of trimethylenediamine interacts simultaneously with 2 centers of the dimeric form of kinase, forming nonequivalent complexes. The covalent attachment of the reagent to 1 subunit of creatine kinase does not prohibit complex formation and covalent binding of bifunctional ATP analogs to the other subunit of the dimer, but results in a 10-fold decrease in affinity of the ATP deriv. for the nonmodified center of the enzyme. These data permit an evaluation of the distance between the ATP-binding sites of creatine kinase in its dimeric form as .apprx.5-6 .ANG.. Such a distance between active sites may be the reason for the higher activity of the M and M' creatine kinase subunits taken sep. as compared to the enzyme dimeric form.

L13 ANSWER 117 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 92879-29-3 REGISTRY

CN Agarose, [6-[[3-[[9-(1,3-diiformyl-6,8,8-trihydroxy-6,8-dioxido-2,5,7-

Searched by: Mary Hale 308-4258 CM-1 12D16

trioxa-6,8-diphosphaoct-1-yl)-9H-purin-6-yl]amino]-1-oxopropyl]amino]hexyl]carbamimidate (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Agarose, [6-[[3-[[9-(1,3-diethyl-6,8,8-trihydroxy-2,5,7-trioxa-6,8-diphosphaoct-1-yl)-9H-purin-6-yl]amino]-1-oxopropyl]amino]hexyl]carbamimidate, P,P'-dioxide

MF C20 H32 N8 O12 P2 . x Unspecified

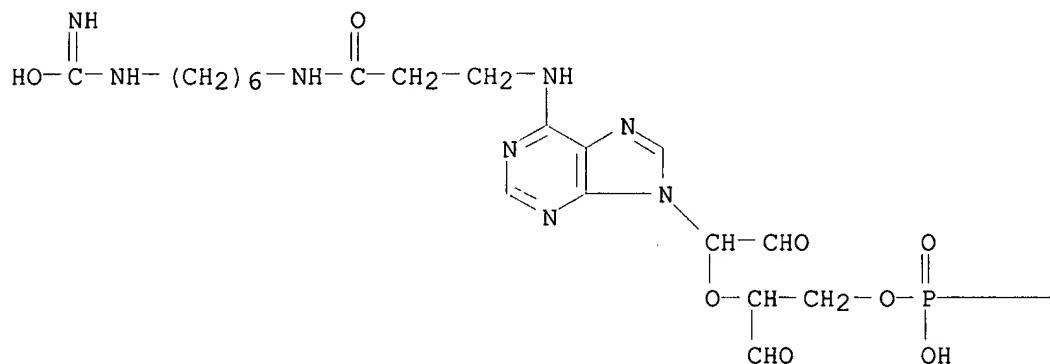
PCT Manual registration

CM 1

CRN 173298-44-7

CMF C20 H32 N8 O12 P2

PAGE 1-A



PAGE 1-B

— OPO₃H₂

CM 2

CRN 9012-36-6

CMF Unspecified

CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L13 ANSWER 118 OF 166 REGISTRY COPYRIGHT 2002 ACS

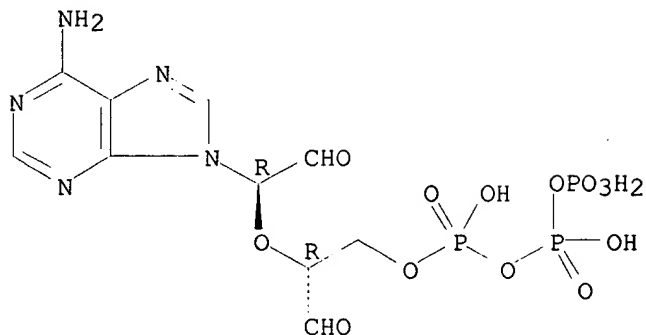
RN 90829-92-8 REGISTRY

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, magnesium salt (1:1), [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Searched by: Mary Hale 308-4258 CM-1 12D16

NAME)
 FS STEREOSEARCH
 MF C10 H14 N5 O13 P3 . Mg
 LC STN Files: CA, CAPLUS
 CRN (54970-91-1)

Absolute stereochemistry.



● Mg

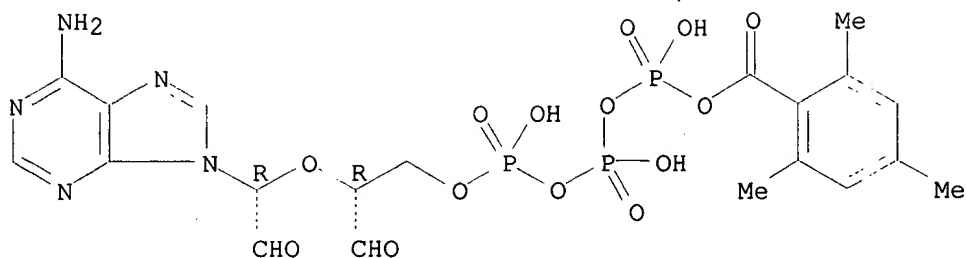
1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 101:35044 Inactivation of beef heart mitochondrial F1-ATPase by the 2',3'-dialdehyde derivatives of adenine nucleotides. Fernandes de Melo, Dirce; Satre, Michel; Vignais, Pierre V. (Lab. Biochim., Cent. Etud. Nucl., Grenoble, 38041, Fr.). FEBS Lett., 169(1), 101-6 (English) 1984. CODEN: FEBLAL. ISSN: 0014-5793.

AB Beef heart mitochondrial F1 ATPase was inactivated by the 2',3'-dialdehyde derivs. of ATP, ADP, and AMP (oATP, oADP, and oAMP, resp.). In the absence of Mg²⁺, inactivation resulted from the binding of 1 mol nucleotide analog/active unit of F1. The most efficient analog was oADP, followed by oAMP and oATP. Complete inactivation was correlated with the binding of .apprx.11 mol [14C]oADP/mol F1. After correction for nonspecific labeling, the no. of specifically bound [14C]oADP was 2-3 mol/mol F1. By SDS-polyacrylamide gel electrophoresis, [14C]oADP was found to bind covalently mainly to the .alpha. and .beta. subunits. In the presence of Mg²⁺, oATP behaved as a substrate and was slowly hydrolyzed.

L13 ANSWER 119 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 89023-64-3 REGISTRY
 CN Benzoic acid, 2,4,6-trimethyl-, P-anhydride with P' '-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] tetrahydrogen (triphosphate), [R-(R*,R*)]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C20 H24 N5 O14 P3
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 100:121507 Synthesis and properties of mixed anhydrides of AMP, ADP and ATP with mesitoic acid. Sokolova, N. I.; Tretyakova, S. S.; Shabarova, Z. A. (Belozerskii Lab. Mol. Biol. Bioorg. Chem., Moscow State Univ., Moscow, 117234, USSR). Nucleosides Nucleotides, 2(3), 203-19 (English) 1983. CODEN: NUNUD5. ISSN: 0732-8311.

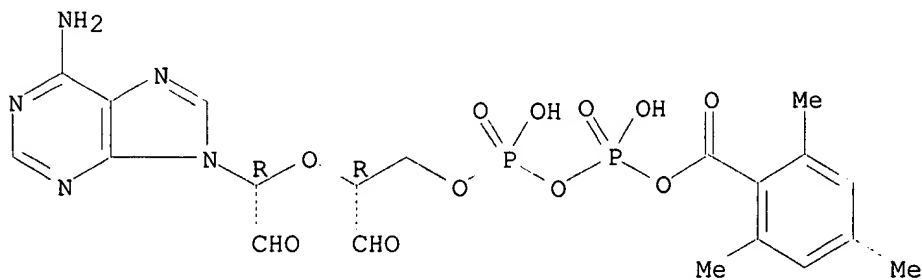
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Optimal conditions for the prepn. of the title anhydrides I (n = 1-3) from the corresponding nucleotides and mesitoic acid were detd. I were oxidized with NaIO₄ to give corresponding dialdehydes II, which were treated with p-N₃C₆H₄CONHNH₂ to give the cyclized products III. Etheno analogs IV were prepd. by treating I with ClCH₂CHO. UV, CD, and fluorescence spectra of the compds. prepd. were analyzed. Hydrolysis of I and IV was carried out over a wide pH range. The compds. prepd. are new affinity reagents for ATP-dependent enzymes.

L13 ANSWER 120 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 89023-63-2 REGISTRY
CN Benzoic acid, 2,4,6-trimethyl-, monoanhydride with P'-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] trihydrogen (diphosphate), [R-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H23 N5 O11 P2
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



Searched by: Mary Hale 308-4258 CM-1 12D16

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 100:121507 Synthesis and properties of mixed anhydrides of AMP, ADP and ATP with mesitoic acid. Sokolova, N. I.; Tretyakova, S. S.; Shabarova, Z. A. (Belozerskii Lab. Mol. Biol. Bioorg. Chem., Moscow State Univ., Moscow, 117234, USSR). Nucleosides Nucleotides, 2(3), 203-19 (English) 1983. CODEN: NUNUD5. ISSN: 0732-8311.

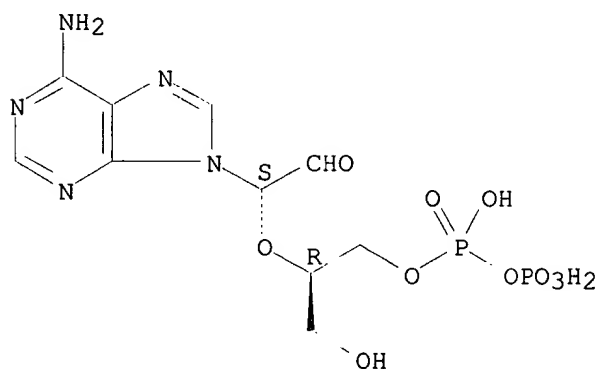
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Optimal conditions for the prepn. of the title anhydrides I (n = 1-3) from the corresponding nucleotides and mesitoyl chloride were detd. I were oxidized with NaIO₄ to give corresponding dialdehydes II, which were treated with p-N₃C₆H₄CONHNH₂ to give the cyclized products III. Etheno analogs IV were prepd. by treating I with ClCH₂CHO. UV, CD, and fluorescence spectra of the compds. prepd. were analyzed. Hydrolysis of I and IV was carried out over a wide pH range. The compds. prepd. are new affinity reagents for ATP-dependent enzymes.

L13 ANSWER 121 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 88169-73-7 REGISTRY
CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-hydroxypropyl] ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H15 N5 O10 P2
LC STN Files: CA, CAPLUS, MEDLINE

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:4052 Some peculiarities of affinity modification of myosin ATPase by the monoaldehyde derivative of ADP. Pron'ko, G. M.; Petushkova, E. V. (M. V. Lomonosov Moscow State Univ., Moscow, USSR). Biokhimiya (Moscow), 56(3), 467-76 (Russian) 1991. CODEN: BIOHAO. ISSN: 0320-9725.

Searched by: Mary Hale 308-4258 CM-1 12D16

AB The highly purified monoaldehyde deriv. of ADP obtained by partial redn. of the dialdehyde deriv. of ADP caused strong irreversible inhibition of the Ca^{2+} -ATPase activity of myosin subfragment 1 (S1), the inhibition being of the affinity modification type. The addn. to the reaction medium of Mg^{2+} (but not Ca^{2+}) during S1 interaction with the inhibitor fully prevented the inhibiting effect with all ATPase used (Ca^{2+} -, Mg^{2+} -, or K^{+} , EDTA-ATPases). In contrast, S1 modified in the absence of Mg^{2+} exhibited the same degree of inhibition for all 3 types of ATPase activity. An unexpected result that was previously unobserved for other affinity modifiers of myosin ATPase was the maintenance of activity in 50% of the active centers, when 2-head forms of the enzyme (myosin proper and heavy meromyosin) were modified. It was noteworthy that the affinity modification reaction was characterized by the same K_i values as in the case of myosin S1 ($K_i = 3.3\text{--}3.5 \times 10^{-4} \text{ M}$; $k_i = 0.03\text{--}0.04 \text{ min}^{-1}$). This finding provided addnl. evidence in favor of the functional asymmetry of myosin heads in the myosin mol. which appears to be due to the screening of the active center of one head by the other.

REFERENCE 2: 100:2714 Affinity labeling of succinyl-CoA synthetase from *Escherichia coli* by the 2',3'-dialdehyde derivative of adenosine 5'-diphosphate. Nishimura, Jonathan S.; Mitchell, Theresa; Collier, Glen E.; Matula, J. Michael; Ball, Dorothy J. (Health-Sci. Cent., Univ. Texas, San Antonio, TX, 78284, USA). *Eur. J. Biochem.*, 136(1), 83-7 (English) 1983. CODEN: EJBCAI. ISSN: 0014-2956.

AB ADP 2',3'-dialdehyde (I) exhibited the properties of an affinity label with *E. coli* succinyl-CoA synthetase (II). Inactivation of II by I followed pseudo-1st-order kinetics and was competitively blocked by ADP. The stoichiometry of labeling of II was 1 mol/mol α . β . or, extrapolated, 2 mol/mol inactive α . β . I also exhibited the properties of a substrate, bringing about rapid dephosphorylation of the enzyme. Further specificity of I was demonstrated in partially inactivated II by selective inhibition of the succinate \rightarrow succinyl-CoA exchange reaction, in comparison to the CoA \rightarrow succinyl-CoA exchange reaction. Modifn. of II by I resulted in crosslinking of the enzyme, casting uncertainty over the subunit binding site for ADP. Modification of II by ADP 2'-semialdehyde occurred at a faster rate than that by I, but exhibited biphasic inhibitor concn. dependence and did not exhibit saturability.

L13 ANSWER 122 OF 166 REGISTRY COPYRIGHT 2002 ACS

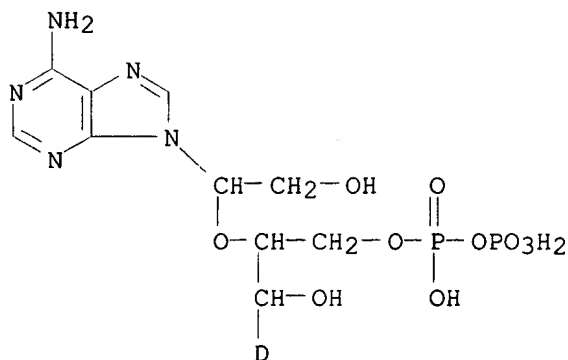
RN 84659-23-4 REGISTRY

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl-3-d] ester (9CI) (CA INDEX NAME)

MF C10 H16 D N5 O10 P2

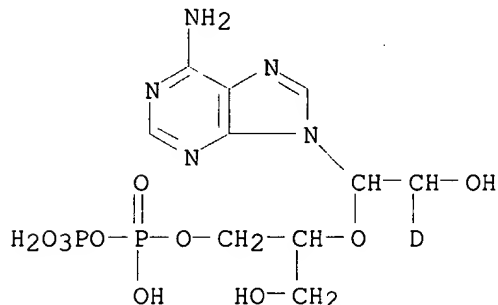
LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

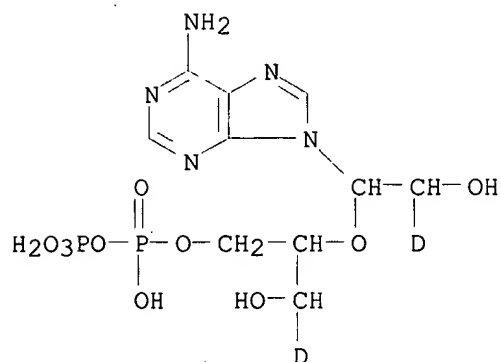
- REFERENCE 1: 98:89799 Borohydride reduction of periodate-oxidized nucleotides; isolation and structure of the reduction intermediate. Rosenthal, Luann P.; Hogenkamp, Harry P. C.; Bodley, James W. (Dep. Biochem., Univ. Minnesota, Minneapolis, MN, 55455, USA). Carbohydr. Res., 111(1), 85-91 (English) 1982. CODEN: CRBRAT. ISSN: 0008-6215.
- AB The redn. of periodate-oxidized nucleotides with NaBH₄ proceeds via a reaction intermediate presumed to be a monoalc. The borohydride-redn. intermediate of periodate-oxidized ADP has been isolated by anion-exchange, liq. chromatog., and subjected to redn. Redn. by NaBH₄ and NaBD₄ showed that the 2 aldehyde groups are sequentially reduced in the order 3' and 2', and that the isolated intermediate corresponds to the semi-reduced, 3'-alc., 2'-aldehyde deriv. This compd. is a useful analog for the study of enzymes and proteins that interact with nucleotides.
- L13 ANSWER 123 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 84659-22-3 REGISTRY
CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy-2-d]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)
MF C10 H16 D N5 O10 P2
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

- REFERENCE 1: 98:89799 Borohydride reduction of periodate-oxidized nucleotides; isolation and structure of the reduction intermediate. Rosenthal, Luann P.; Hogenkamp, Harry P. C.; Bodley, James W. (Dep. Biochem., Univ. Minnesota, Minneapolis, MN, 55455, USA). Carbohydr. Res., 111(1), 85-91 (English) 1982. CODEN: CRBRAT. ISSN: 0008-6215.
- AB The redn. of periodate-oxidized nucleotides with NaBH₄ proceeds via a reaction intermediate presumed to be a monoalc. The borohydride-redn. intermediate of periodate-oxidized ADP has been isolated by anion-exchange, liq. chromatog., and subjected to redn. Redn. by NaBH₄ and NaBD₄ showed that the 2 aldehyde groups are sequentially reduced in the order 3' and 2', and that the isolated intermediate corresponds to the semi-reduced, 3'-alc., 2'-aldehyde deriv. This compd. is a useful analog for the study of enzymes and proteins that interact with nucleotides.
- L13 ANSWER 124 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 84659-21-2 REGISTRY
CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy-2-d]-3-hydroxypropyl-3-d] ester (9CI) (CA INDEX NAME)
MF C10 H15 D2 N5 O10 P2

LC STN Files: BEILSTEIN*, CA, CAPLUS
 (*File contains numerically searchable property data)



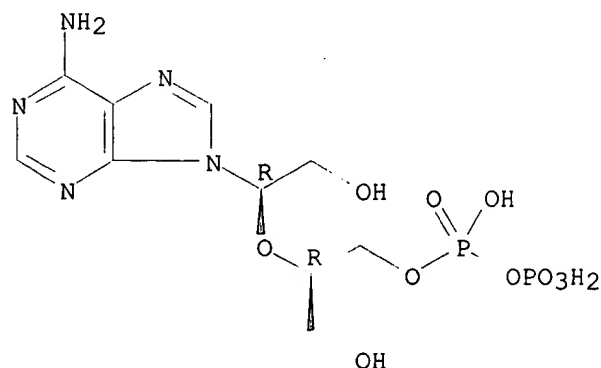
1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 98:89799 Borohydride reduction of periodate-oxidized nucleotides; isolation and structure of the reduction intermediate. Rosenthal, Luann P.; Hogenkamp, Harry P. C.; Bodley, James W. (Dep. Biochem., Univ. Minnesota, Minneapolis, MN, 55455, USA). Carbohydr. Res., 111(1), 85-91 (English) 1982. CODEN: CRBRAT. ISSN: 0008-6215.

AB The redn. of periodate-oxidized nucleotides with NaBH4 proceeds via a reaction intermediate presumed to be a monoalc. The borohydride-redn. intermediate of periodate-oxidized ADP has been isolated by anion-exchange, liq. chromatog., and subjected to redn. Redn. by NaBH4 and NaBD4 showed that the 2 aldehyde groups are sequentially reduced in the order 3' and 2', and that the isolated intermediate corresponds to the semi-reduced, 3'-alc., 2'-aldehyde deriv. This compd. is a useful analog for the study of enzymes and proteins that interact with nucleotides.

L13 ANSWER 125 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 84230-56-8 REGISTRY
 CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C10 H17 N5 O10 P2
 LC STN Files: BEILSTEIN*, CA, CAPLUS
 (*File contains numerically searchable property data)

Absolute stereochemistry.



Searched by: Mary Hale 308-4258 CM-1 12D16

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

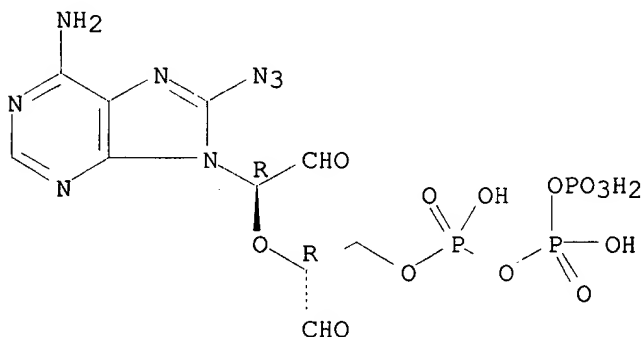
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 98:49500 Phenol sulfotransferase. II. Inactivation by phenylglyoxal, N-ethylmaleimide and ribonucleotide 2',3'-dialdehydes. Borchardt, Ronald T.; Schasteen, Charles S.; Wu, Su Er (Smissman Res. Lab., Univ. Kansas, Lawrence, KS, 66045, USA). Biochim. Biophys. Acta, 708(3), 280-93 (English) 1982. CODEN: BBACAQ. ISSN: 0006-3002.

AB Phenylglyoxal rapidly inactivated rat liver phenol sulfotransferase (EC 2.8.2.1) (I). Enzyme inactivation was accompanied by incorporation of 1.5 mol [7-¹⁴C]phenylglyoxal/mol enzyme. 3'-Phosphoadenosine 5'-phosphosulfate (PAPS), the sulfate donor, prevented inactivation and decreased [7-¹⁴C]phenylglyoxal incorporation to 0.78 mol/mol enzyme. N-Ethylmaleimide also caused rapid inactivation of I with concomitant incorporation of 2.35 mol N-[³H]ethylmaleimide/mol enzyme. Thus, arginine residues may be anionic recognition sites for PAPS, and essential SH residues are present on phenol sulfotransferase. Ribonucleotide dialdehydes, but not the corresponding 2',3'-acyclic nucleotides, produced rapid and irreversible inactivation of I. These ribonucleotide dialdehydes modify the active site of the enzyme, as inclusion of PAPS, or the product, adenosine 3',5'-diphosphate, prevented loss of I activity. p-Nitrophenol did not show similar protective effects. Kinetic studies indicated that the ribonucleotide dialdehydes inactivated the enzyme via a unimol. reaction within a dissociable enzyme-inhibitor complex rather than via a nonspecific bimol. process. Apparently, ribonucleotide dialdehydes are affinity labeling reagents for I, causing enzyme inactivation by the possible formation of a Schiff base adduct with an active-site lysine residue.

L13 ANSWER 126 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 83700-69-0 REGISTRY
CN Triphosphoric acid, P-[2-[1-(6-amino-8-azido-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H13 N8 O13 P3
LC STN Files: CA, CAPLUS, MEDLINE

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 97:211502 Photoaffinity labeling of the .beta. subunit of phosphorylase kinase by 8-azidoadenosine 5'-triphosphate and its 2',3'-dialdehyde derivative. King, Marita M.; Carlson, Gerald M.; Haley,

Searched by: Mary Hale 308-4258 CM-1 12D16

Boyd E. (Dep. Chem., Univ. South Florida, Tampa, FL, 33620, USA). J. Biol. Chem., 257(23), 14058-65 (English) 1982. CODEN: JBCHA3. ISSN: 0021-9258.

AB Photoaffinity labeling of rabbit skeletal muscle phosphorylase kinase (I) in the presence of micromolar concns. of [γ - 32 P]8-azidoadenosine 5'-triphosphate (II) resulted in preferential labeling of its β subunit. Protection from incorporation of II into I was afforded by ADP, ATP, and oATP (ATP 2',3'-dialdehyde). In the presence of Ca^{2+} and Mg^{2+} , but in the absence of photolysis, II could be utilized as a substrate for autophosphorylation and phosphorylase conversion, which demonstrated that Mg -II binds to a catalytic site on I. Several effectors, or changes in labeling conditions, strongly influenced affinity labeling of I by II. When photolabeling was carried out with nonactivated I at pH 8.2, or with autophosphorylated enzyme at pH 6.8, 2 conditions known to activate the enzyme, there was a similar decrease in the amt. of labeling. A decrease in labeling was also obsd. in the presence of Ca^{2+} and(or) Mg^{2+} . The 2',3'-dialdehyde deriv. of II (III) also preferentially labeled the β subunit of I. In the absence of photolysis, III mimicked previously reported interactions of I with oATP: responsiveness to the synergistic action of Ca^{2+} and Mg^{2+} , exhibition of a similar K_i , and the ability to serve as a substrate. Photoincorporation of III showed the same sensitivity toward metal ions that was obsd. with II, and labeling was substantially decreased in the presence of nonradioactive II, suggesting that these 2 analogs may be competing for the same binding site(s).

L13 ANSWER 127 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 82339-88-6 REGISTRY

CN β -Alanine, N-[8-bromo-9-(1,3-diformyl-6,8,8-trihydroxy-6,8-dioxido-2,5,7-trioxa-6,8-diphosphaoct-1-yl)-9H-purin-6-yl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

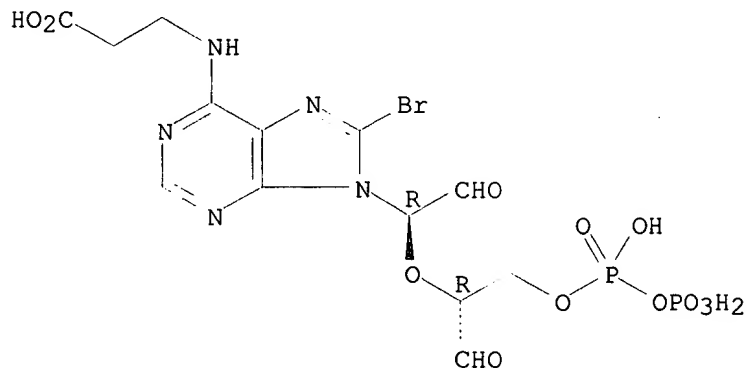
CN β -Alanine, N-[8-bromo-9-(1,3-diformyl-6,8,8-trihydroxy-2,5,7-trioxa-6,8-diphosphaoct-1-yl)-9H-purin-6-yl]-, P,P'-dioxide, [R-(R*,R*)]-

FS STEREOSEARCH

MF C13 H16 Br N5 O12 P2

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

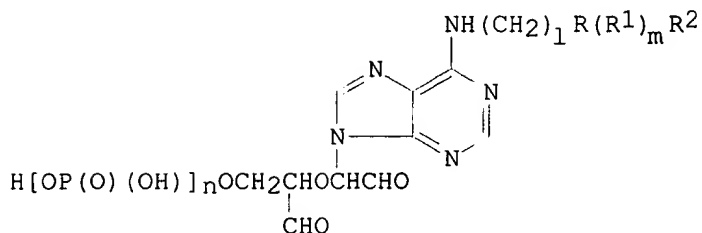
1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 97:106259 Enzyme immobilization. (Unitika Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 57039783 A2 19820305 Showa, 5 pp. (Japanese).

Searched by: Mary Hale 308-4258 CM-1 12D16

GI



AB A substrate for enzyme immobilization, I, consists of an adenosine deriv. in which R is CONH or CO₂, R₁ is alkyl, arom., or cycloalkyl, and R₂ is a high-mol.-wt. support; l = 1 or 2, m = 0 or 1, and n = 1-3. Thus, 5 g Sepharose 4B was swelled in H₂O, activated with CNBr, and suspended in 0.1M NaHSO₃. 8-Bromo-N⁶-carboxyethyl-ADP (200 mg) was added and allowed to react for 12 h at 4.degree.. The gel was then washed, resuspended in 50 mL H₂O, and treated with 6 mL 0.5M Na metaperiodate for 1 h at room temp. The treated gel with its ribose 2',3'-dialdehyde deriv. of ADP as a substituent was then washed, suspended in 50 mL 0.1M phosphate buffer, pH 8.5, and mixed with 10 mL of a soln. of Bacillus stearothermophilus acetate kinase in the same buffer. The support immobilized 61,000 of 100,000 units applied; a sample of CH-Sepharose 4B taken for comparison immobilized only 4,000 of 20,000 units applied.

L13 ANSWER 128 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 82086-45-1 REGISTRY

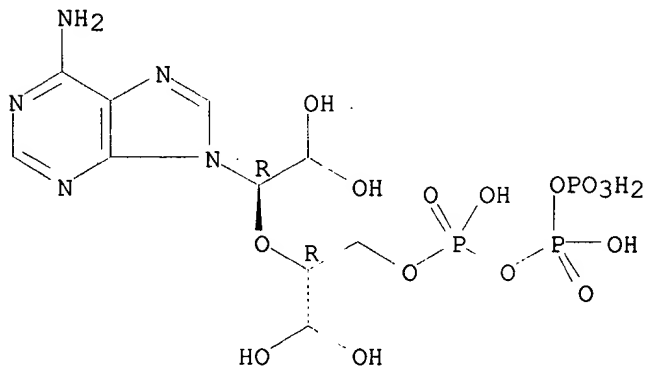
CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2,2-dihydroxyethoxy]-3,3-dihydroxypropyl] ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C10 H18 N5 O15 P3

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 97:24150 Preparation, structure, and properties of periodate-oxidized ATP, a potential affinity-labeling reagent. Lowe,

Searched by: Mary Hale 308-4258 CM-1 12D16

Peter N.; Beechey, R. Brian (Dep. Biochem., Chelsea Coll., London, SW3 6LX, UK). Bioorg. Chem., 11(1), 55-71 (English) 1982. CODEN: BOCMBM. ISSN: 0045-2068.

AB Periodate oxidn. of ATP yields a single product which was purified and characterized. Periodate-oxidized ATP (o-ATP) behaves as a single compd. during TLC anal., but NMR spectral studies show that it exists in aq. soln. as an equil. mixt. of 3 dialdehyde monohydrates and a dihydrate. Little free aldehyde is present. The dialdehyde monohydrates are in the form of diastereomeric cyclic hemiacetals. The dialdehyde grouping of o-ATP was reduced with NaBH₄, producing a diol. O-ATP is frequently used in attempts to affinity label nucleotide-binding sites on proteins. The proposed structure of o-ATP is discussed in relation to this use for o-ATP.

L13 ANSWER 129 OF 166 REGISTRY COPYRIGHT 2002 ACS

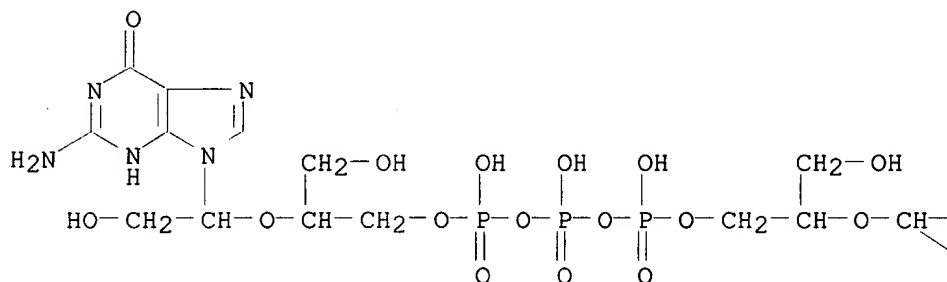
RN 81523-95-7 REGISTRY

CN Triphosphoric acid, P-[2-[1-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] P''-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, stereoisomer (9CI) (CA INDEX NAME)

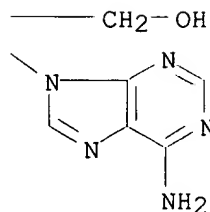
MF C20 H31 N10 O17 P3

LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 1-B



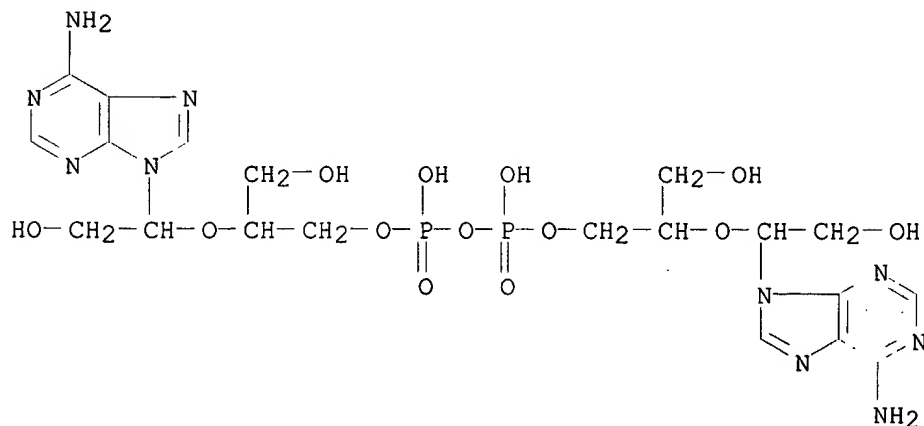
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

- REFERENCE 1: 97:177129 Catabolic properties of 5',5''-linked dinucleoside phosphates in rat liver nuclei. Bornemann, Siegmars; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Z. Naturforsch., C: Biosci., 37C(9), 818-23 (German) 1982. CODEN: ZNCBDA. ISSN: 0341-0382.
- AB The enzymic degrdn. of ¹⁴C-labeled 5',5''-linked dinucleoside triphosphates Gp3A, 2-O-methylGp3A, 2'dGp3A, 2',3'-dideoxyGp3A, and 7-methylGp3A in rat liver nuclei was studied. The 2'-deoxy- and 2',3'-dideoxy compds. are poorer substrates than the other cap-structured dinucleotides investigated.
- REFERENCE 2: 96:177213 High-performance liquid-chromatographic method for separation of dinucleotides. Hagemeyer, Eberhard; Bornemann, Siegmars; Boos, Karl Siegfried; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). J. Chromatogr., 237(1), 174-7 (English) 1982. CODEN: JOCRAM. ISSN: 0021-9673.
- AB Nucleotides were sepd. by high-performance liq. chromatog. (HPLC) at 24.degree. on 2 different systems, and uses of the methods are described for sepg. cap-structured dinucleotides and related compds., monitoring the progress of dinucleotide synthesis, and purity control of naturally occurring and synthesized compds. HPLC was performed on (A) a 300 .times. 2.3 mm column packed with Nucleosil 10 SB (10 .mu.m) or on (B) a 250 .times. 3.2 mm column of Partisil PAC (10 .mu.m). The mobile phase for system A was 0.1M KNO₃-0.02M KH₂PO₄ (pH 2.6), and mobile phases for system B were (B1) 0.8M NH₄ formate buffer (pH 4.1), or (B2) 0.4M NH₄ formate buffer (pH 4.1), or (B3) a 6- min linear gradient from water up to 0.8M NH₄ formate (pH 4.1). Retention times are given for the sepn. of various nucleotides and dinucleoside di-, tri-, tetra-, and pentaphosphates. A very rapid and selective sepn., however, of all nucleotides studied was achieved by the use of system B with linear gradient elution with B3. System A was used to monitor the reaction course of Gp3A synthesis, and system B3 was used to analyze a synthesized Gp3A peak for purity and yield.
- L13 ANSWER 130 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 81523-93-5 REGISTRY
 CN Diphosphoric acid, P,P'-bis[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, stereoisomer (9CI) (CA INDEX NAME)
 MF C20 H30 N10 O13 P2
 LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 96:177213 High-performance liquid-chromatographic method for separation of dinucleotides. Hagemeyer, Eberhard; Bornemann, Siegmund; Boos, Karl Siegfried; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). J. Chromatogr., 237(1), 174-7 (English) 1982. CODEN: JOCRAM. ISSN: 0021-9673.

AB Nucleotides were sep'd. by high-performance liq. chromatog. (HPLC) at 24.degree. on 2 different systems, and uses of the methods are described for sepg. cap-structured dinucleotides and related compds., monitoring the progress of dinucleotide synthesis, and purity control of naturally occurring and synthesized compds. HPLC was performed on (A) a 300 .times. 2.3 mm column packed with Nucleosil 10 SB (10 .mu.m) or on (B) a 250 .times. 3.2 mm column of Partisil PAC (10 .mu.m). The mobile phase for system A was 0.1M KNO3-0.02M KH2PO4 (pH 2.6), and mobile phases for system B were (B1) 0.8M NH4 formate buffer (pH 4.1), or (B2) 0.4M NH4 formate buffer (pH 4.1), or (B3) a 6- min linear gradient from water up to 0.8M NH4 formate (pH 4.1). Retention times are given for the sepn. of various nucleotides and dinucleoside di-, tri-, tetra-, and pentaphosphates. A very rapid and selective sepn., however, of all nucleotides studied was achieved by the use of system B with linear gradient elution with B3. System A was used to monitor the reaction course of Gp3A synthesis, and system B3 was used to analyze a synthesized Gp3A peak for purity and yield.

L13 ANSWER 131 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 78195-29-6 REGISTRY

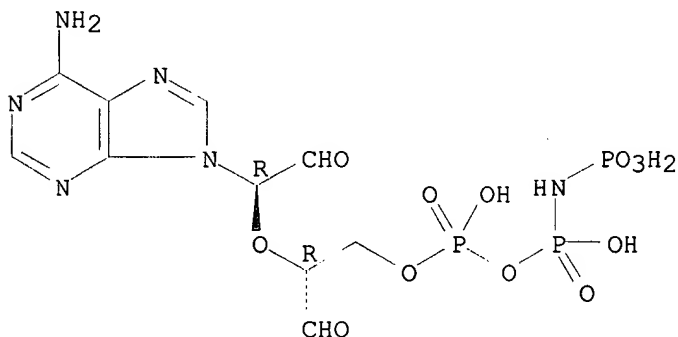
CN Imidotriphosphoric acid, P'--[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C10 H15 N6 O12 P3

LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 95:145941 Potent inhibition of membrane-bound rat intestinal alkaline phosphatase by a new series of phosphate analogs. Shirazi, Soraya P.; Beechey, R. Brian; Butterworth, Peter J. (Dep. Biochem., Chelsea Coll., London, SW3 6LX, Engl.). Biochem. J., 194(3), 797-802

Searched by: Mary Hale 308-4258 CM-1 12D16

(English) 1981. CODEN: BIJOAK. ISSN: 0306-3275.

- AB Alk. phosphatase (EC 3.1.3.1) of rat intestinal brush-border membrane vesicles was competitively inhibited at pH 7.5 by phenylene-1,3-diphosphonate, 2,6-dinitrophenylphosphonate, and phosphonoacetaldehyde with K_i of 16-80 μM . β -Thio-ADP and γ -thio-ATP were potent, mainly competitive inhibitors ($K_i = 10 \mu\text{M}$) with a slight noncompetitive element. β - γ -Imido-ATP was a competitive inhibitor, but oxidn. of the ribose moiety with NaIO_4 resulted in an active-site-directed irreversible inhibitor that could be of general use in studies of the enzyme mechanism.

REFERENCE 2: 95:57056 Interaction of phosphorylase kinase with the 2',3'-dialdehyde derivative of adenosine triphosphate. 1. Kinetics of inactivation. King, Marita M.; Carlson, Gerald M. (Dep. Chem., Univ. South Florida, Tampa, FL, 33620, USA). Biochemistry, 20(15), 4382-7 (English) 1981. CODEN: BICHAW. ISSN: 0006-2960.

- AB The 2',3'-dialdehyde deriv. of ATP (oATP) was found to be a valid affinity label for rabbit skeletal muscle phosphorylase kinase. Inactivation by oATP at pH 6.8 followed pseudo-1st-order and satn. kinetics. An apparent K_i of $\text{apprx.} 6.7 \mu\text{M}$ was obtained in the presence of 0.6 mM Ca^{2+} plus 10 mM Mg^{2+} . Protection against the rate of inactivation was provided by the natural substrate ATP. In addn., at pH 8.2 oATP could be used as a substrate to phosphorylate phosphorylase b, thus providing evidence that oATP can bind to the active site of phosphorylase kinase. Inactivation of phosphorylase kinase by oATP was sensitive to various effectors of the enzyme such as Ca^{2+} , Mg^{2+} , and pH. Ca^{2+} plus Mg^{2+} synergistically enhanced the rate of inactivation several-fold; each metal ion by itself had little effect on the rate of inactivation. This synergism was seen both at pH 6.8 and at pH 8.2; however, the rates of inactivation were much greater at pH 6.8. The enhancement of inactivation by Ca^{2+} plus Mg^{2+} was also more pronounced with activated than with nonactivated kinase.

L13 ANSWER 132 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 75521-15-2 REGISTRY

CN Pyridinium, 3-(aminocarbonyl)-1-[13-(6-amino-9H-purin-9-yl)-1,3,11,13-tetraformyl-6,8-dihydroxy-6,8-dioxido-2,5,7,9,12-pentaoxa-6,8-diphosphatridec-1-yl]-, inner salt, [1R-(1R*,3R*,11R*,13R*)]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Pyridinium, 3-(aminocarbonyl)-1-[13-(6-amino-9H-purin-9-yl)-1,3,11,13-tetraformyl-6,8-dihydroxy-2,5,7,9,12-pentaoxa-6,8-diphosphatridec-1-yl]-, inner salt, P,P'-dioxide, [1R-(1R*,3R*,11R*,13R*)]-

FS STEREOSEARCH

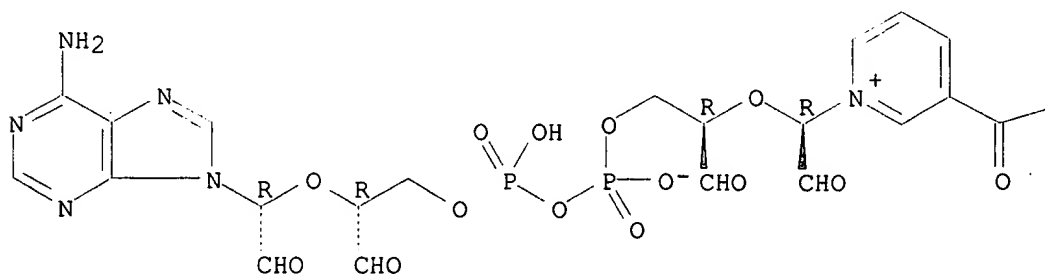
MF C21 H23 N7 O14 P2

CI COM

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



—NH₂

4 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:154918 Assimilatory nitrate reductase: reduction and inhibition by NADH/NAD⁺ analogs. Trimboli, Anthony J.; Barber, Michael J. (Department of Biochemistry and Molecular Biology, University of South Florida, Tampa, FL, 33612, USA). Arch. Biochem. Biophys., 315(1), 48-53 (English) 1994. CODEN: ABBIA4. ISSN: 0003-9861.

AB Assimilatory nitrate reductase from *Chlorella vulgaris* catalyzes the rate-limiting step, the conversion of nitrate to nitrite, in nitrate assimilation. Initial rate studies of nitrate reductase activity, performed under optimum conditions of const. ionic strength (μ = 0.2) and pH (8.0) and using NADH as reductant, indicated the absence of substrate inhibition at NADH concns. below 300 μ M and NO₃⁻ concns. less than 3 mM. *Chlorella* nitrate reductase exhibited a marked preference for NADH (V_{max} = 9.2 μ mol NADH/min/nmol heme and K_m = 2.3 μ M) as the physiol. electron donor but could also utilize α -NADH (V_{max} = 5.6 μ mol NADH/min/nmol heme and K_m = 131 μ M) and NADPH (V_{max} = 0.6 μ mol NADPH/min/nmol heme and K_m = 910 μ M) through with significantly decreased efficiency. Examn. of various NADH-analogs indicated that reduced nicotinamide hypoxanthine dinucleotide (NHDH) was used most efficiently (V_{max} = 9.3 μ mol NHDH/min/nmol heme and K_m = 7.9 μ M), while reduced NMN (NMNH) was utilized least efficiently (V_{max} = 0.07 μ mol NMNH/min/nmol heme and K_m = 676 μ M). Overall, modifications to the nicotinamide moiety or the addn. of a phosphate group were obsd. to result in the most significant decreases in V_{max} , indicating poor reducing substrates. Product inhibition studies indicated both NAD⁺ (K_i = 2.2 mM) and NADP⁺ (K_i = 10.5 mM) to be competitive inhibitors of *Chlorella* NR. A variety of NAD⁺ analogs were also detd. to act as competitive inhibitors with varying degrees of efficiency. 3-Pyridinealdehyde adenine dinucleotide was the most efficient inhibitor (K_i = 0.74 mM) while nicotinamide was the least efficient (K_i = 18.1 mM). Overall, changing substituents on the nicotinamide ring or its complete deletion produced the most effective inhibitors compared to NAD⁺. In contrast, changes in the adenine or ribose moieties produced less effective inhibitors when compared to NAD⁺. These results represent the most comprehensive anal. of the effect of modifications of the physiol. reductant (NADH) and product (NAD⁺) on nitrate reductase activity.

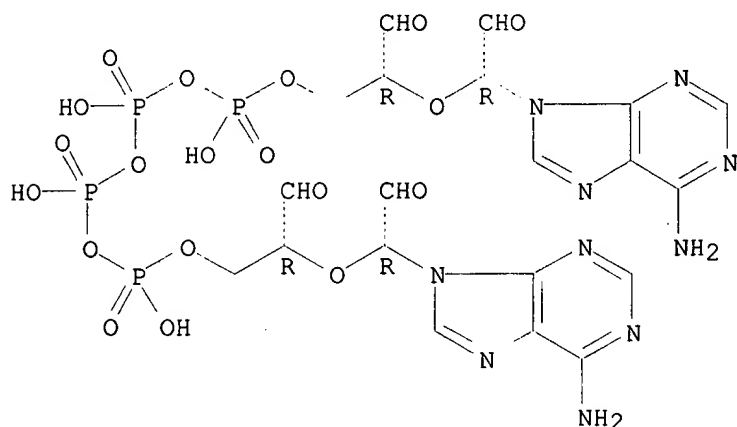
REFERENCE 2: 111:227852 Affinity modification of microsomal flavoproteins by NAD(P) 2',3'-dialdehydes. Slepneva, I. A.; Weiner, L. M. (Inst. Chem. Kinet. Combust., Novosibirsk, 630090, USSR). Biochem. Biophys. Res. Commun., 164(2), 758-63 (English) 1989. CODEN: BBRCA9. ISSN: 0006-291X.

AB NADPH-cytochrome P 450 reductase (FP1) and NADH-cytochrome b5 reductase (FP2) involved in the microsomal fraction of rat liver were modified chem. by periodate-oxidized NADP and NAD [o-NAD(P)]. Despite its low K_i (\approx 30 μ M) o-NADP is not covalently bound with FP1, although o-NAD with K_i > 100 μ M chem. modifies FP1 by suppressing its activity. The protective effect of NADP against FP1 inactivation indicates that FP1 is modified in the NADPH binding site. An active center of FP2 is modified by o-NAD in the same manner as FP1 (NAD prevents FP2 from inactivation). FP2 is slightly inactivated when the concn. of o-NADP is one order of

magnitude higher than that of o-NAD. The o-NAD-modified microsomal FP1 inhibits the oxidn. of cytochrome P 450 substrates (acetanilide and p-nitroanisole).

- REFERENCE 3: 109:207461 Affinity modification of NADPH-cytochrome P-450 reductase. Slepneva, I. A.; Weiner, L. M. (Inst. Chem. Kinet. Combust., Novosibirsk, 630090, USSR). Biochem. Biophys. Res. Commun., 155(2), 1026-32 (English) 1988. CODEN: BBRC9. ISSN: 0006-291X.
- AB The active center of NADPH-cytochrome P 450 reductase (EC 1.6.2.4) contains the lysine residue essential for catalytic activity. Chem. modification of the .epsilon.-amino group of this lysine residue is the subject of the present study. To modify the .epsilon.-amino group, periodate-oxidized NADP and NAD (o-NAD(P)) were employed. Both reagents appeared to be competitive inhibitors of NADPH-cytochrome P 450 reductase (K_i for o-NADP .apprx.10 .mu.M, K_i for o-NAD >100 .mu.M). However, o-NADP does not share a covalent bond with the reductase, whereas o-NAD modifies the reductase at the binding site of NADPH. A protective effect of NADP and the labeling extent close to unity (0.7) upon reductase inactivation indicate the affinity type of modification. The different results of reductase modification by either o-NADP or o-NAD may be due to the difference in the structures of the analogs bound to the enzyme active site.
- REFERENCE 4: 93:217110 Simple immobilization method for NAD(+) with the preservation of coenzyme activity. Schoepp, W.; Lorenz, Rita (Ber. Biochem., Karl-Marx-Univ. Leipzig, Leipzig, 7010, Ger. Dem. Rep.). Acta Biol. Med. Ger., 39(2-3), 335-7 (German) 1980. CODEN: ABMGAJ. ISSN: 0001-5318.
- AB NAD was oxidized by periodate and immobilized on an adipic acid dihydrazide-Sepharose 4B conjugate by means of the aldehyde groups formed. The substitution degree of the NAD-Sepharose was between 0.26 and 0.82 .mu.mol NAD/mL Sepharose gel. At least 90% of the immobilized NAD could be reduced by NaBH₄. The immobilized coenzyme was active in the reaction with alc. dehydrogenase and EtOH; .apprx.30% of the coenzyme was reduced in the enzymic reaction at pH 8.0 in 0.067M phosphate buffer. The immobilized coenzyme prepn. is relatively sensitive to hydrolysis; after 14 days storage in water at 4.degree., the enzymically reducible portion of coenzyme was decreased to 50% the original value.
- L13 ANSWER 133 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 75042-77-2 REGISTRY
CN Tetraphosphoric acid, P,P'''-bis[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [2R-[1[R*(R*)],2R*(R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H24 N10 O19 P4
CI COM
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:80241 Specific dinucleoside polyphosphate cleaving enzymes from chromaffin cells: a fluorimetric study. Ramos, Antonio; Rotllan, Pedro (Departamento de Bioquímica y Biología Molecular, Universidad de La Laguna, 38206 La Laguna, Tenerife, Canary Islands, Spain). Biochim. Biophys. Acta, 1253(1), 103-11 (English) 1995. CODEN: BBACAQ. ISSN: 0006-3002.

AB This article presents a fluorimetric study of the main properties of the enzymes dinucleoside tetraphosphate (asym.) hydrolase or dinucleoside tetraphosphatase (Ap4Aase, EC 3.6.1.17) and dinucleoside triphosphate hydrolase or dinucleoside triphosphatase (Ap3Aase, EC 3.6.1.29), both present in adrenal medulla cytosolic exts. Diethenoadenosine polyphosphates, .epsilon.-(ApnA), are used as artificial fluorogenic substrates. Ap4Aase exhibits a mol. mass around 20 kDa and neutral optimum pH (7.0-7.5). It requires Mg²⁺ and preferentially hydrolyzes substrates with four phosphate groups. Km for .epsilon.-(Ap4A) is 1.3 .mu.M and Ki for Ap4A and Gp4G are 1 and 0.2 .mu.M resp. Km for Ap4A detd. by HPLC is 1.6 .mu.M. .epsilon.-(Ap5A) and .epsilon.-(Ap6A) are hydrolyzed at reduced rates. This enzyme is inhibited by Zn²⁺, F⁻ and very strongly by Ap4 and .epsilon.-Ap4. Ca²⁺ cannot replace Mg²⁺, but behaves as inhibitor in its presence. The substrate analogs dinucleoside triphosphates Ap3A, Gp3G, m7Gp3G and m7Gp3A and the periodate-oxidized nucleotides o-(Ap4A), o.epsilon.-(Ap4A), o-Ap4 and o.epsilon.-Ap4 behave as inhibitors. Ap3Aase exhibits a mol. mass around 30 kDa and neutral optimum pH (7.0-7.5). It requires Mg²⁺ or Ca²⁺, but retains a low measurable activity around 10% in the absence of these divalent cations. It only hydrolyzes substrates with three phosphate groups. Km for .epsilon.-(Ap3A) is 11 .mu.M and Ki for Ap3A and Gp3G are 20 and 22 .mu.M, resp. Km for Ap3A detd. by HPLC is 16 .mu.M. m7Gp3G and m7Gp3A are also good substrates for triphosphatase.

REFERENCE 2: 93:165266 Intracellular signals of proliferation control: diadenosine tetraphosphate (Ap4A) - a trigger of DNA replication. Grummt, F. (Max-Planck-Inst. Biochem., Munich, D-8033, Fed. Rep. Ger.). Control Mech. Anim. Cells: Specific Growth Factors, [Pap. Round Table], Meeting Date 1979, 109-19. Editor(s): Jimenez de Asua, Luis; Levi-Montalcini, Rita; Shields, Robert. Raven: New York, N. Y. (English) 1980. CODEN: 43WHA2.

AB Diadenosine tetraphosphate (Ap4A) was able to induce DNA replication in

G1-arrested BHK cells in vitro and was bound to the 57,000-dalton subunit of DNA polymerase .alpha. (I) in a dose-dependent manner. The covalent binding of oxidized Ap4A to I inactivated the enzyme. The capability of rat cerebral neurons to bind Ap4A declined during development (5 days before to 60 days after birth) with a similar rate as did the I activity, indicating a specific correlation between the level of replicating activity and the Ap4A-binding capacity in neuronal cells. Methylene-bis-ADP(II), a structural analog of Ap4A, competed at a 1:1 ratio with Ap4A for its binding site at I. Methylene-bis-AMP was inactive, whereas ADP competed only at a 100-fold excess with Ap4A for its binding site. DNA synthesis in vitro was strongly inhibited by II. In both 3T3 and SV40-transformed 3T3, methylene-bis-5'-AMP inhibited in vivo DNA synthesis from [3H]thymidine. The addn. of methylene-bis-adenosine to the cultures not only completely inhibited DNA replication but also the proliferation of these cells.

L13 ANSWER 134 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 74427-36-4 REGISTRY

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

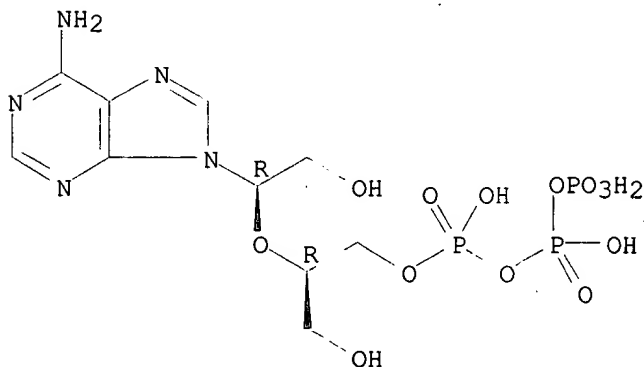
CN Triphosphoric acid, P-[2-[(1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy)-3-hydroxypropyl] ester, [R-(R*,R*)]-

FS STEREOSEARCH

MF C10 H18 N5 O13 P3

LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)

4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:344793 Capping DNA with DNA. Li, Yingfu; Liu, Yong; Breaker, Ronald R. (Department of Molecular Cellular and Developmental Biology, Yale University, New Haven, CT, 06520-8103, USA). Biochemistry, 39(11), 3106-3114 (English) 2000. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB Twelve classes of deoxyribozymes that promote an ATP-dependent "self-capping" reaction were isolated by in vitro selection from a random-sequence pool of DNA. Each deoxyribozyme catalyzes the transfer of the AMP moiety of ATP to its 5'-terminal phosphate group, thereby forming a 5',5'-pyrophosphate linkage. An identical DNA adenylate structure is generated by the T4 DNA ligase during enzymic DNA ligation. A

Searched by: Mary Hale 308-4258 CM-1 12D16

41-nucleotide class 1 deoxyribozyme requires Cu^{2+} as a cofactor and adopts a structure that recognizes both the adenine and triphosphate moieties of ATP or dATP. The catalytic efficiency for this DNA, measured at $10^4 \text{ M}^{-1} \cdot \text{cnt} \cdot \text{min}^{-1}$ using either ATP or dATP as substrate, is similar to other catalytic nucleic acids that use small substrates. Chem. probing and site-directed mutagenesis implicate the formation of guanine quartets as crit. components of the active structure. The observation of ATP-dependent "self-charging" by DNA suggests that DNA could be made to perform the reactions typically assocd. with DNA cloning, but without the assistance of protein enzymes.

REFERENCE 2: 106:63465 Nucleoside 5'-triphosphates modified at sugar residues as substrates for calf thymus terminal deoxynucleotidyl transferase and for AMV reverse transcriptase. Bibilashvilli, R. S.; Skamrov, A. V.; Kutateladze, T. V.; Mazo, A. M.; Kraevskii, A. A.; Kukhanova, M. K. (Natl. Cardiol. Res. Cent., Moscow, USSR). *Biochim. Biophys. Acta*, 868(2-3), 136-44 (English) 1986. CODEN: BBACAQ. ISSN: 0006-3002.

AB Terminal deoxynucleotidyltransferase from calf thymus and AMV (avian myeloblastosis virus) RNA-directed DNA polymerase (reverse transcriptase) catalyze the incorporation of 3'-amino-2',3'-dideoxynucleoside 5'-triphosphates, as well as some of their 3'-derivs., e.g., 3'-amino-3'-deoxyarabinonucleoside 5'-triphosphates, and some other nucleoside 5'-triphosphates modified at sugar residues. After incorporation of the appropriate 5'-mononucleotide residue into the DNA, further chain elongation is blocked. This finding opens up the possibility of selective inhibition of DNA synthesis catalyzed by a certain enzyme.

REFERENCE 3: 98:49500 Phenol sulfotransferase. II. Inactivation by phenylglyoxal, N-ethylmaleimide and ribonucleotide 2',3'-dialdehydes. Borchardt, Ronald T.; Schasteen, Charles S.; Wu, Su Er (Smismman Res. Lab., Univ. Kansas, Lawrence, KS, 66045, USA). *Biochim. Biophys. Acta*, 708(3), 280-93 (English) 1982. CODEN: BBACAQ. ISSN: 0006-3002.

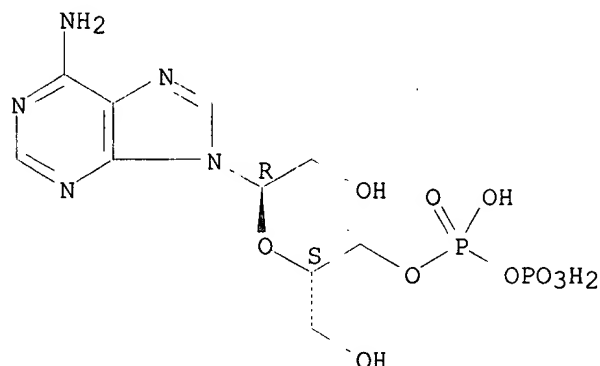
AB Phenylglyoxal rapidly inactivated rat liver phenol sulfotransferase (EC 2.8.2.1) (I). Enzyme inactivation was accompanied by incorporation of 1.5 mol [7- ^{14}C]phenylglyoxal/mol enzyme. 3'-Phosphoadenosine 5'-phosphosulfate (PAPS), the sulfate donor, prevented inactivation and decreased [7- ^{14}C]phenylglyoxal incorporation to 0.78 mol/mol enzyme. N-Ethylmaleimide also caused rapid inactivation of I with concomitant incorporation of 2.35 mol N-[3H]ethylmaleimide/mol enzyme. Thus, arginine residues may be anionic recognition sites for PAPS, and essential SH residues are present on phenol sulfotransferase. Ribonucleotide dialdehydes, but not the corresponding 2',3'-acyclic nucleotides, produced rapid and irreversible inactivation of I. These ribonucleotide dialdehydes modify the active site of the enzyme, as inclusion of PAPS, or the product, adenosine 3',5'-diphosphate, prevented loss of I activity. p-Nitrophenol did not show similar protective effects. Kinetic studies indicated that the ribonucleotide dialdehydes inactivated the enzyme via a unimol. reaction within a dissociable enzyme-inhibitor complex rather than via a nonspecific bimol. process. Apparently, ribonucleotide dialdehydes are affinity labeling reagents for I, causing enzyme inactivation by the possible formation of a Schiff base adduct with an active-site lysine residue.

REFERENCE 4: 93:63716 On the chemical communication between the mitochondrial adenine nucleotide carrier and its substrate. Schlimme, Eckhard; Boos, Karl Siegfried; De Groot, Egon Jabbo (Lab. Biol. Chem. Fachber. Naturwiss., Univ. Paderborn, Paderborn, Fed. Rep. Ger.). *Mol. Mech. Biol. Recognition*, Proc. Aharon Katzir-Katchalsky Conf., Meeting Date 1978, 443-8. Editor(s): Balaban, Miriam. Elsevier: Amsterdam, Neth. (English) 1979. CODEN: 43GWAZ.

AB The effect of base, sugar, or phosphate group modification of adenine nucleotides on the carrier protein-mediated translocation mechanism were studied to elucidate the structural requirements of the adenine nucleotide which are essential for recognition by the membrane-bound receptor (carrier-specific binding) and addnl. required to trigger the transfer. Structural modifications of the adenine base were tolerated by the adenine nucleotide carrier, an integral lipoprotein of the inner mitochondrial membrane, with respect to binding and exchange, provided that the electron distributions in the heterocycle, including an unmodified C6-amino group, were retained, i.e. the adenine character of the base remained unchanged. Modification of the phosphate chain had only moderate influence on carrier-specific binding and exchange, provided that the no. of neg. charges in the phosphate chain was unchanged. Modified nucleotide substrates with a conformation equiv. to that of ATP (anti, gauche, gauche) could not be accommodated in the carrier binding site and the transfer did not occur. The D-configuration of the ribose had to remain unchanged; no inversion of chirality was tolerated by the carrier with the exception of the 3'-hydroxyl group which could be substituted by H. The 2'-hydroxyl group was necessary for the bound nucleotide to trigger the transmembrane adenine nucleotide exchange.

L13 ANSWER 135 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 73566-18-4 REGISTRY
 CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, labeled with carbon-14, [S-(R*,S*)]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C10 H17 N5 O10 P2
 LC STN Files: CA, CAPLUS
 IL XC-14

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 93:39691 P1,P3-[5'-guanosyl-5''-[14C]-adenosyl]triphosphate: preparation of the cap parent compound and its catabolism by rat liver subcellular fractions. Bornemann, Siegmund; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Gesamthochsch. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Z. Naturforsch., C: Biosci., 35C(1-2), 57-64 (German) 1980. CODEN: ZNCBDA. ISSN: 0341-0382.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The chem. synthesis of P1,P3-(5'-guanosyl-5''-[14C]adenosyl)triphosphate (labeled I), which is the labeled parent compd. of 5'-terminal cap structures of most eukaryotic mRNA's, as well as of noncap structures and derivs. is described. I and the noncap-structured nucleotide Ap2A-14C (II), as well as their labeled ribose-ring-opened derivs., III and IV, resp., were incubated with rat liver nuclei, mitochondria, and other subcellular fractions. The nucleases present in the nuclear fraction preferentially degraded I over the other structures, whereas there was no such preference in degrdn. by mitochondria, 500 g supernatant (homogenate minus nuclei), or 15,000 g supernatant. Evidently, cap-degrading nucleases able to unblock 5'-termini of mRNA are present in liver nuclei but not mitochondria. Also, an intact ribofuranoside system in the dinucleoside triphosphates is apparently required by the cap-degrading nucleases.

L13 ANSWER 136 OF 166 REGISTRY COPYRIGHT 2002 ACS

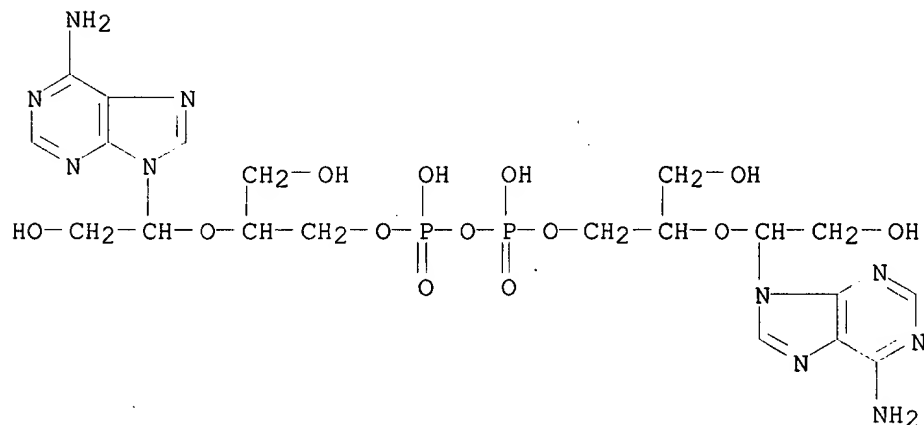
RN 73566-15-1 REGISTRY

CN Diphosphoric acid, P,P'-bis[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, labeled with carbon-14, stereoisomer (9CI) (CA INDEX NAME)

MF C20 H30 N10 O13 P2

LC STN Files: CA, CAPLUS

IL XC-14



1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 93:39691 P1,P3-[5'-guanosyl-5''-[14C]-adenosyl]triphosphate: preparation of the cap parent compound and its catabolism by rat liver subcellular fractions. Bornemann, Siegmund; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Gesamthochsch. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Z. Naturforsch., C: Biosci., 35C(1-2), 57-64 (German) 1980. CODEN: ZNCBDA. ISSN: 0341-0382.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

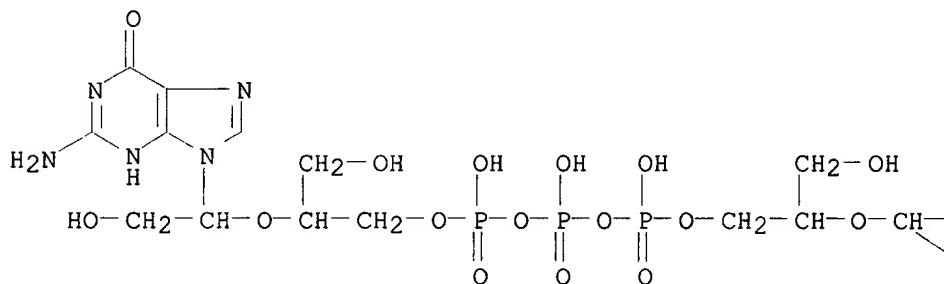
AB The chem. synthesis of P1,P3-(5'-guanosyl-5''-[14C]adenosyl)triphosphate (labeled I), which is the labeled parent compd. of 5'-terminal cap

Searched by: Mary Hale 308-4258 CM-1 12D16

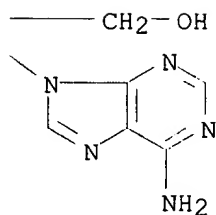
structures of most eukaryotic mRNA's, as well as of noncap structures and derivs. is described. I and the noncap-structured nucleotide Ap2A-14C (II), as well as their labeled ribose-ring-opened derivs., III and IV, resp., were incubated with rat liver nuclei, mitochondria, and other subcellular fractions. The nucleases present in the nuclear fraction preferentially degraded I over the other structures, whereas there was no such preference in degrdn. by mitochondria, 500 g supernatant (homogenate minus nuclei), or 15,000 g supernatant. Evidently, cap-degrading nucleases able to unblock 5'-termini of mRNA are present in liver nuclei but not mitochondria. Also, an intact ribofuranoside system in the dinucleoside triphosphates is apparently required by the cap-degrading nucleases.

L13 ANSWER 137 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 73566-13-9 REGISTRY
 CN Triphosphoric acid, P-[2-[1-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] P''-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, labeled with carbon-14, stereoisomer (9CI) (CA INDEX NAME)
 MF C20 H31 N10 O17 P3
 LC STN Files: CA, CAPLUS
 IL XC-14

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 93:39691 P1,P3-[5'-guanosyl-5''-[14C]-adenosyl]triphosphate: preparation of the cap parent compound and its catabolism by rat liver subcellular fractions. Bornemann, Siegmund; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Gesamthochsch. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Z. Naturforsch., C: Biosci., 35C(1-2), 57-64 (German) 1980. CODEN: ZNCBDA. ISSN: 0341-0382.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The chem. synthesis of P1,P3-(5'-guanosyl-5''-[14C]adenosyl)triphosphate (labeled I), which is the labeled parent compd. of 5'-terminal cap structures of most eukaryotic mRNA's, as well as of noncap structures and derivs. is described. I and the noncap-structured nucleotide Ap2A-14C (II), as well as their labeled ribose-ring-opened derivs., III and IV, resp., were incubated with rat liver nuclei, mitochondria, and other subcellular fractions. The nucleases present in the nuclear fraction preferentially degraded I over the other structures, whereas there was no such preference in degrdn. by mitochondria, 500 g supernatant (homogenate minus nuclei), or 15,000 g supernatant. Evidently, cap-degrading nucleases able to unblock 5'-termini of mRNA are present in liver nuclei but not mitochondria. Also, an intact ribofuranoside system in the dinucleoside triphosphates is apparently required by the cap-degrading nucleases.

L13 ANSWER 138 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 72710-15-7 REGISTRY

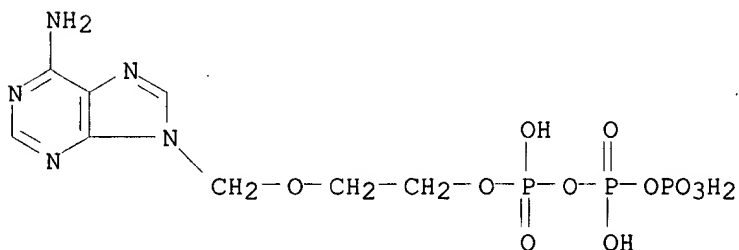
CN Triphosphoric acid, P-[2-[(6-amino-9H-purin-9-yl)methoxy]ethyl] ester (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C8 H14 N5 O11 P3

LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:261845 Three-dimensional microarray system for parallel genotyping of single nucleotide polymorphisms by PCR. Klimecki, Walter (Motorola Inc., USA). PCT Int. Appl. WO 2001021838 A2 20010329, 17 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG,

Searched by: Mary Hale 308-4258 CM-1 12D16

SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US25988 20000922. PRIORITY: US 1999-PV155431 19990922.

AB The present invention provides methods for detecting nucleic acid mutations and genetic polymorphisms by single base extension anal. Specifically, the invention provides an app. and methods for the detection of single base extension of a particular oligonucleotide in an oligonucleotide microarray following hybridization between oligonucleotides bound to defined regions of a polymeric hydrogel-based microarray and nucleic acids in a biol. sample.

REFERENCE 2: 92:76842 Synthesis and circular dichroism spectra of dinucleoside phosphate-analogs containing 1-(.beta.-hydroxyethoxymethyl)cytosine and 9-(.beta.-hydroxyethoxymethyl)adenine. Tychinskaya, L. Yu.; Lysov, Yu. P.; Florent'ev, V. L. (Inst. Mol. Biol., Moscow, USSR). Bioorg. Khim., 5(7), 1059-70 (Russian) 1979. CODEN: BIKHD7.

AB Analogs of dinucleoside phosphates were synthesized contg. 1-(2-hydroxyethoxymethyl)cytosine (CytMeOEtOH) and 9-(2-hydroxyethoxymethyl)adenine (AdeMeOEtOH) either at the 3'- or 5'-end, e.g. AdeMeOEtO-P-Ado (Ado = adenosine), Ado-P OEtOMeAde, CytMeOEtO-P-Ado, Cyt-P-OEtOMeAde, or Ado-P-OEtOMeCyt. Addnl. mono- and triphosphates of CytMeOEtOH and AdeMeOEtOH were prepd. The temp. dependence of CD spectra of dinucleoside phosphate analogs was examd. (0.1M phosphate buffer, pH 7; 6.4M LiCl) and thermodyn. parameters for the equil. described by a 2-state model were detd. The contribution of the ether O of the ribose ring to the organization and stabilization of the single-stranded helix of oligonucleotides was discussed.

L13 ANSWER 139 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 71997-43-8 REGISTRY

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, trisodium salt, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

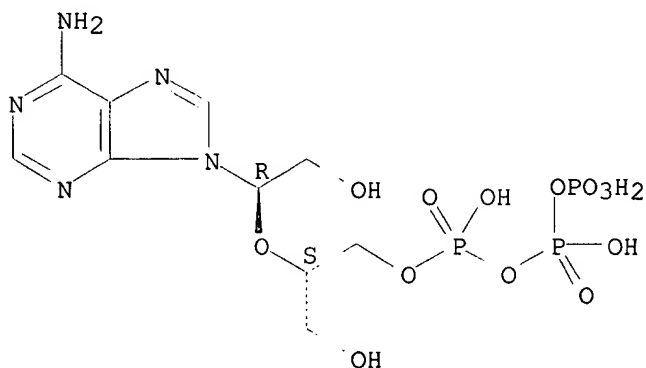
FS STEREOSEARCH

MF C10 H18 N5 O13 P3 . 3 Na

LC STN Files: CA, CAPLUS

CRN (35677-98-6)

Absolute stereochemistry.



3 Na

1 REFERENCES IN FILE CA (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 92:1735 Mitochondrial adenine nucleotide carrier.

Investigation of principal structural, steric, and contact requirements for substrate binding and transport by means of ribose-modified substrate analogs. Boos, Karl Siegfried; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Biochemistry, 18(24), 5304-9 (English) 1979. CODEN: BICHAW. ISSN: 0006-2960.

AB A selected series of 14 ribose-modified adenine nucleotide analogs was prepd. and characterized as the .alpha.-32P- or U-14C-labeled compds. The capacity of rat liver mitochondria for adenine nucleotide carrier-linked (specific) binding and carrier-mediated transfer across the inner mitochondrial membrane as well as the amt. of noncarrier-linked (unspecific) binding of these analogs was detd. at 5.degree. by an inhibitor (atractyloside) stop-method and compared with these values with the natural substrates ADP and ATP. Kinetic data of carrier-specific bound analogs were evaluated from Dixon plots and indicate that these analogs act as competitive inhibitors for mitochondrial ADP and ATP uptake. The findings confirm the distinct substrate specificity of the carrier system. By use of the analogs, an exptl. proof of the 2-step nature of mitochondrial adenine nucleotide translocation, i.e., carrier-specific binding (recognition) and transport, was obtained. Furthermore, the findings provide a detailed description of the basic steric, contact, and structural elements which are prerequisite for carrier-specific binding (A) and addnl. for subsequent transport (B): (A) (1) an anti- or syn-positioned .beta.-N-glycosyl-linked purine base; (2) an S- or N-type sugar pucker; (3) a cis disposition of the C(4')-C(5') bond with respect to the heterocycle; (B) (1) a nonfixed anti-positioned purine base with a N-glycosyl torsion angle of .apprx.-20.degree.; (2) an S-type sugar pucker; (3) a gauche-gauche orientation of the exocyclic C(5')-O(5') group; and (4) a trans-positioned [C(2') ribo] hydroxyl group, which presumably triggers the induction of carrier-mediated transport.

L13 ANSWER 140 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 71997-42-7 REGISTRY

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, disodium salt, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

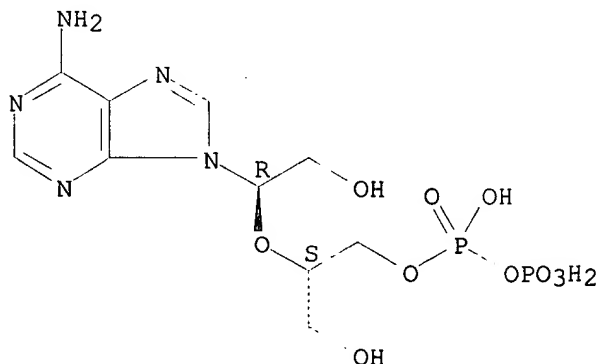
FS STEREOSEARCH

MF C10 H17 N5 O10 P2 . 2 Na

LC STN Files: CA, CAPLUS

CRN (58176-57-1)

Absolute stereochemistry.



2 Na

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 92:1735 Mitochondrial adenine nucleotide carrier.

Investigation of principal structural, steric, and contact requirements for substrate binding and transport by means of ribose-modified substrate analogs. Boos, Karl Siegfried; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Biochemistry, 18(24), 5304-9 (English) 1979. CODEN: BICHAW. ISSN: 0006-2960.

AB A selected series of 14 ribose-modified adenine nucleotide analogs was prepd. and characterized as the .alpha.-32P- or U-14C-labeled compds. The capacity of rat liver mitochondria for adenine nucleotide carrier-linked (specific) binding and carrier-mediated transfer across the inner mitochondrial membrane as well as the amt. of noncarrier-linked (unspecific) binding of these analogs was detd. at 5.degree. by an inhibitor (atractyloside) stop-method and compared with these values with the natural substrates ADP and ATP. Kinetic data of carrier-specific bound analogs were evaluated from Dixon plots and indicate that these analogs act as competitive inhibitors for mitochondrial ADP and ATP uptake. The findings confirm the distinct substrate specificity of the carrier system. By use of the analogs, an exptl. proof of the 2-step nature of mitochondrial adenine nucleotide translocation, i.e., carrier-specific binding (recognition) and transport, was obtained. Furthermore, the findings provide a detailed description of the basic steric, contact, and structural elements which are prerequisite for carrier-specific binding (A) and addnl. for subsequent transport (B): (A) (1) an anti- or syn-positioned .beta.-N-glycosyl-linked purine base; (2) an S- or N-type sugar pucker; (3) a cis disposition of the C(4')-C(5') bond with respect to the heterocycle; (B) (1) a nonfixed anti-positioned purine base with a N-glycosyl torsion angle of .apprx.-20.degree.; (2) an S-type sugar pucker; (3) a gauche-gauche orientation of the exocyclic C(5')-O(5') group; and (4) a trans-positioned [C(2') ribo] hydroxyl group, which presumably triggers the induction of carrier-mediated transport.

L13 ANSWER 141 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 71997-40-5 REGISTRY

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, trisodium salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, trisodium salt, [R-(R*,R*)]-

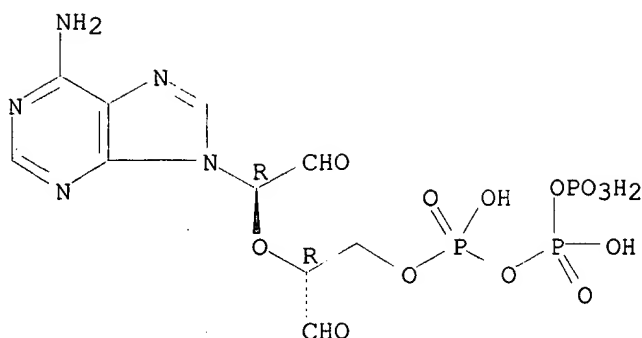
FS STEREOSEARCH

MF C10 H14 N5 O13 P3 . 3 Na

LC STN Files: CA, CAPLUS, CHEMCATS

CRN (54970-91-1)

Absolute stereochemistry.



● 3 Na

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:202393 Complexities of measuring antagonist potency at P2X7 receptor orthologs. Hibell, A. D.; Thompson, K. M.; Xing, M.; Humphrey, P. P. A.; Michel, A. D. (Glaxo Institute of Applied Pharmacology, Department of Pharmacology, University of Cambridge, Cambridge, UK). Journal of Pharmacology and Experimental Therapeutics, 296(3), 947-957 (English) 2001. CODEN: JPETAB. ISSN: 0022-3565. Publisher: American Society for Pharmacology and Experimental Therapeutics.

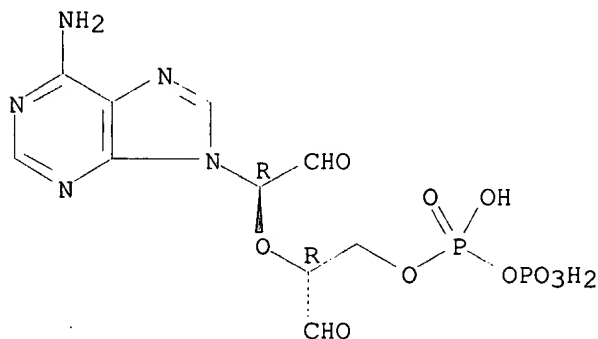
AB The ability of P2 antagonists to affect agonist-stimulated fluorescent dye accumulation in cells expressing human, rat, or mouse P2X7 receptors was examd. Several compds., including pyridoxalphosphate-6-azophenyl-2',4'-disulfonic acid (PPADS), which was previously thought to be a weak P2X7 receptor antagonist, possessed high potency (nanomolar IC50) at human and rat P2X7 receptors. However, there were species differences in antagonist potency with PPADS, pyridoxal 5'-phosphate (P5P), and periodate-oxidized ATP (OxATP) exhibiting 20- to 500-fold higher potency for human than for mouse P2X7 receptors. HMA (5-(N,N-hexamethylene)amiloride) was also selective for human over rat P2X7 receptors but potentiated responses at mouse P2X7 receptors. Coomassie Brilliant Blue G (CBB) was a nonselective antagonist with high potency at mouse P2X7 receptors (IC50 .apprx. 100 nM). All compds. were noncompetitive antagonists, and potency could only be quantified by measuring IC50 values. These values were similar when detd. against EC50 concns. of ATP or 2'- and 3'-O-4(-benzoylbenzoyl)-ATP and, for most compds., only slightly (3- to 5-fold) affected by agonist concn. However, IC50 values for KN62 (1-[N,O-bis(5-isoquinolinesulfonyl)-N-methyl-L-tyrosyl]-4-phe nylpiperazine) and suramin, varied up to 25-fold depending upon agonist concn. Furthermore, IC50 values for KN62 and OxATP were 10-fold lower at 22.degree. than at 37.degree., whereas IC50 values for PPADS, P5P, suramin, and OxATP were up to 20-fold lower in NaCl than in sucrose buffer. Potency ests. for CBB and PPADS decreased 5-fold in the presence of bovine serum albumin, possibly due to protein binding. Given the species differences, and the effects of assay conditions on antagonist potency, caution must be exercised when interpreting results obtained with the available antagonists.

REFERENCE 2: 92:1735 Mitochondrial adenine nucleotide carrier. Investigation of principal structural, steric, and contact requirements for substrate binding and transport by means of ribose-modified substrate analogs. Boos, Karl Siegfried; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Biochemistry, 18(24), 5304-9 (English) 1979. CODEN: BICHAW. ISSN: 0006-2960.

AB A selected series of 14 ribose-modified adenine nucleotide analogs was prepd. and characterized as the .alpha.-32P- or U-14C-labeled compds. The capacity of rat liver mitochondria for adenine nucleotide carrier-linked (specific) binding and carrier-mediated transfer across the inner mitochondrial membrane as well as the amt. of noncarrier-linked (unspecific) binding of these analogs was detd. at 5.degree. by an inhibitor (atractyloside) stop-method and compared with these values with the natural substrates ADP and ATP. Kinetic data of carrier-specific bound analogs were evaluated from Dixon plots and indicate that these analogs act as competitive inhibitors for mitochondrial ADP and ATP uptake. The findings confirm the distinct substrate specificity of the carrier system. By use of the analogs, an exptl. proof of the 2-step nature of mitochondrial adenine nucleotide translocation, i.e., carrier-specific binding (recognition) and transport, was obtained. Furthermore, the findings provide a detailed description of the basic steric, contact, and structural elements which are prerequisite for carrier-specific binding (A) and addnl. for subsequent transport (B): (A) (1) an anti- or syn-positioned .beta.-N-glycosyl-linked purine base; (2) an S- or N-type sugar pucker; (3) a cis disposition of the C(4')-C(5') bond with respect to the heterocycle; (B) (1) a nonfixed anti-positioned purine base with a N-glycosyl torsion angle of .apprx.-20.degree.; (2) an S-type sugar pucker; (3) a gauche-gauche orientation of the exocyclic C(5')-O(5') group; and (4) a trans-positioned [C(2') ribo] hydroxyl group, which presumably triggers the induction of carrier-mediated transport.

L13 ANSWER 142 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 71997-39-2 REGISTRY
 CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, disodium salt, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C10 H13 N5 O10 P2 . 2 Na
 LC STN Files: CA, CAPLUS, CHEMCATS
 CRN (64060-84-0)

Absolute stereochemistry.



● 2 Na

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 92:1735 Mitochondrial adenine nucleotide carrier.
 Investigation of principal structural, steric, and contact requirements for substrate binding and transport by means of ribose-modified substrate analogs. Boos, Karl Siegfried; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Biochemistry, 18(24),

Searched by: Mary Hale 308-4258 CM-1 12D16

5304-9 (English) 1979. CODEN: BICHAW. ISSN: 0006-2960.

AB A selected series of 14 ribose-modified adenine nucleotide analogs was prepd. and characterized as the .alpha.-³²P- or U-¹⁴C-labeled compds. The capacity of rat liver mitochondria for adenine nucleotide carrier-linked (specific) binding and carrier-mediated transfer across the inner mitochondrial membrane as well as the amt. of noncarrier-linked (unspecific) binding of these analogs was detd. at 5.degree. by an inhibitor (atractyloside) stop-method and compared with these values with the natural substrates ADP and ATP. Kinetic data of carrier-specific bound analogs were evaluated from Dixon plots and indicate that these analogs act as competitive inhibitors for mitochondrial ADP and ATP uptake. The findings confirm the distinct substrate specificity of the carrier system. By use of the analogs, an exptl. proof of the 2-step nature of mitochondrial adenine nucleotide translocation, i.e., carrier-specific binding (recognition) and transport, was obtained. Furthermore, the findings provide a detailed description of the basic steric, contact, and structural elements which are prerequisite for carrier-specific binding (A) and addnl. for subsequent transport (B): (A) (1) an anti- or syn-positioned .beta.-N-glycosyl-linked purine base; (2) an S- or N-type sugar pucker; (3) a cis disposition of the C(4')-C(5') bond with respect to the heterocycle; (B) (1) a nonfixed anti-positioned purine base with a N-glycosyl torsion angle of .apprx.-20.degree.; (2) an S-type sugar pucker; (3) a gauche-gauche orientation of the exocyclic C(5')-O(5') group; and (4) a trans-positioned [C(2') ribo] hydroxyl group, which presumably triggers the induction of carrier-mediated transport.

L13 ANSWER 143 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 66443-33-2 REGISTRY

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[7-[9-[(6-aminohexyl)amino]-9H-purin-9-yl]-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahept-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[7-[9-[(6-aminohexyl)amino]-9H-purin-9-yl]-1,3-dihydroxy-2,4-dioxo-1,3-diphosphahept-1-yl]-.beta.-D-ribofuranosyl]-, inner salt, P,P'-dioxide

FS STEREOSEARCH

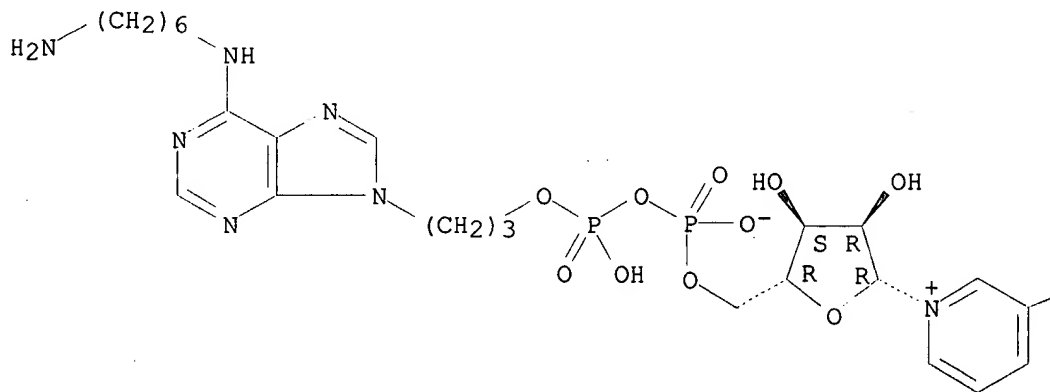
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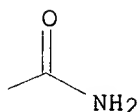
LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)

Absolute stereochemistry.

PAGE 1-A

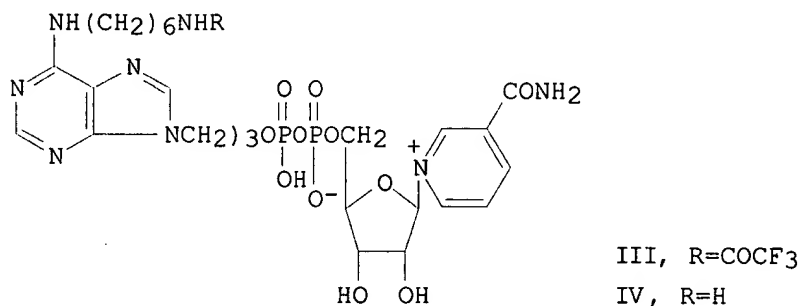
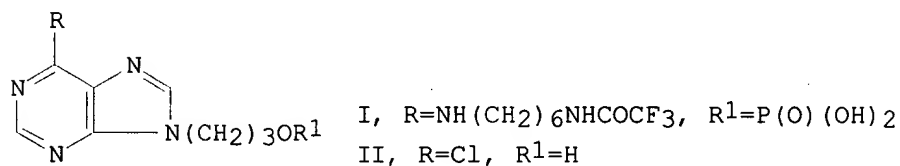




1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 88:185183 The coenzyme analog (3-[6-(6-aminohexylamino)-9-purinyllpropyl)(nicotinamide-D-ribose)diphosphate as ligand for affinity chromatography of dehydrogenases. Berariu, Veronica; Jeck, Reinhard; Woenckhaus, Christoph (Gustav-Embden-Zent. Biol. Chem., Univ. Frankfurt, Frankfurt/Main, Ger.). Justus Liebigs Ann. Chem. (1), 118-23 (German) 1978. CODEN: JLACBF. ISSN: 0075-4617.

GI



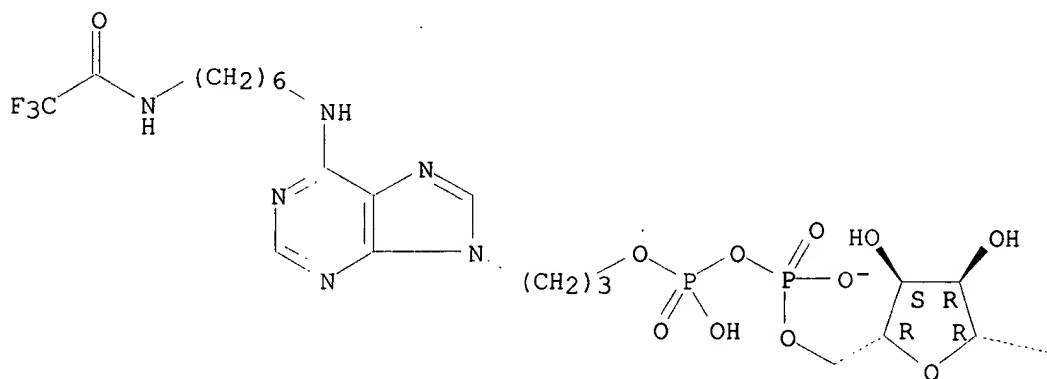
AB 9-[3-(Dihydroxyphosphoryloxy)propyl]-6-[6-(trifluoroacetylaminohexylamino)-9H-purine (I)] was prepd. starting from 6-chloro-9-(3-hydroxypropyl)-9H-purine (II). After condensation of this AMP-analog with dicyclohexylcarbodiimide and NMN in aq. pyridine, a new NAD-analog was formed. The coenzyme analog (3-[6-(6-trifluoroacetylaminohexylamino)-9-purinyllpropyl)(nicotinamide-D-ribose)diphosphate (III) acted as H acceptor (its reduced form as H donor) when tested against different dehydrogenases. Highly disscod. complexes between this coenzyme analog and dehydrogenases were formed. Removal of the trifluoroacetyl group led to the unstable coenzyme analog (3-[6-(6-aminohexylamino)-9-purinyllpropyl)(nicotinamide-D-ribose)diphosphate (IV), which can be covalently attached to agarose activated with CNBr. When dehydrogenases

were applied to the column of the immobilized AMP and NAD-analogs, only glyceraldehyde 3-phosphate dehydrogenase was retained. Elution of the enzyme occurred only after addn. of KCl to the eluant.

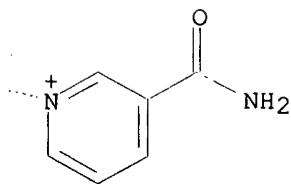
L13 ANSWER 144 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 66443-32-1 REGISTRY
 CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[hydroxy[[hydroxy[3-[6-[[6-
 [(trifluoroacetyl)amino]hexyl]amino]-9H-purin-9-
 yl]propoxy]phosphinyl]oxy]phosphinyl]-.beta.-D-ribofuranosyl]-, inner salt
 (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C27 H37 F3 N8 O12 P2
 LC STN Files: BEILSTEIN*, CA, CAPLUS
 (*File contains numerically searchable property data)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



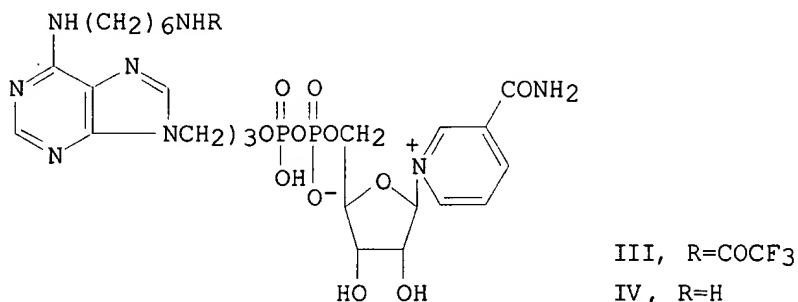
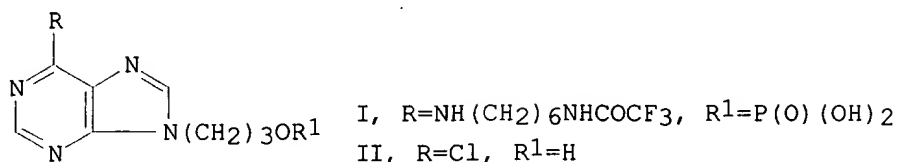
1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 88:185183 The coenzyme analog (3-[6-(6-aminohexylamino)-9-purinyl]propyl)(nicotinamide-D-ribose)diphosphate as ligand for affinity chromatography of dehydrogenases. Berariu, Veronica; Jeck, Reinhard;

Searched by: Mary Hale 308-4258 CM-1 12D16

Woenckhaus, Christoph (Gustav-Embden-Zent. Biol. Chem., Univ. Frankfurt, Frankfurt/Main, Ger.). Justus Liebigs Ann. Chem. (1), 118-23 (German) 1978. CODEN: JLACBF. ISSN: 0075-4617.

GI



AB 9-[3-(Dihydroxyphosphoryloxy)propyl]-6-[6-(trifluoroacetyl-amino)hexylamino]-9H-purine (I) was prepd. starting from 6-chloro-9-(3-hydroxypropyl)-9H-purine (II). After condensation of this AMP-analog with dicyclohexylcarbodiimide and NMN in aq. pyridine, a new NAD-analog was formed. The coenzyme analog (3-[6-(6-trifluoroacetylaminohexylamino)-9-purinyl]propyl)(nicotinamide-D-ribose)diphosphate (III) acted as H acceptor (its reduced form as H donor) when tested against different dehydrogenases. Highly dissocd. complexes between this coenzyme analog and dehydrogenases were formed. Removal of the trifluoroacetyl group led to the unstable coenzyme analog (3-[6-(6-aminohexylamino)-9-purinyl]propyl)(nicotinamide-D-ribose)diphosphate (IV), which can be covalently attached to agarose activated with CNBr. When dehydrogenases were applied to the column of the immobilized AMP and NAD-analogs, only glyceraldehyde 3-phosphate dehydrogenase was retained. Elution of the enzyme occurred only after addn. of KCl to the eluant.

L13 ANSWER 145 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 64060-84-0 REGISTRY

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [R-(R*,R*)]-

OTHER NAMES:

CN ADP 2',3'-dialdehyde

CN oADP

CN ro-ADP

CN roADP

FS STEREOSEARCH

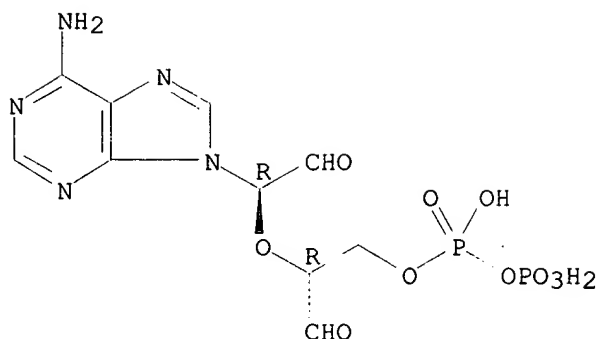
MF C10 H13 N5 O10 P2

CI COM

LC STN Files: BEILSTEIN*, CA, CAPLUS, MEDLINE, TOXCENTER, USPATFULL
 (*File contains numerically searchable property data)

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

34 REFERENCES IN FILE CA (1967 TO DATE)

34 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:97153 Characterization of the NAD⁺ binding site of *Candida boidinii* formate dehydrogenase by affinity labelling and site-directed mutagenesis. Labrou, Nikolas E.; Rigden, Danyel J.; Clonis, Yannis D. (Laboratory of Enzyme Technology, Department of Agricultural Biotechnology, Agricultural University of Athens, Athens, GR-11855, Greece). European Journal of Biochemistry, 267(22), 6657-6664 (English) 2000. CODEN: EJBCAI. ISSN: 0014-2956. Publisher: Blackwell Science Ltd..

AB The 2',3'-dialdehyde deriv. of ADP (oADP) has been shown to be an affinity label for the NAD⁺ binding site of recombinant *Candida boidinii* formate dehydrogenase (FDH). Inactivation of FDH by oADP at pH 7.6 followed biphasic pseudo first-order satn. kinetics. The rate of inactivation exhibited a nonlinear dependence on the concn. of oADP, which can be described by reversible binding of reagent to the enzyme ($K_d = 0.46$ mM for the fast phase, 0.45 mM for the slow phase) prior to the irreversible reaction, with max. rate consts. of 0.012 and 0.007 min⁻¹ for the fast and slow phases, resp. Inactivation of formate dehydrogenase by oADP resulted in the formation of an enzyme-oADP product, a process that was reversed after dialysis or after treatment with 2-mercaptoethanol (> 90% reactivation). The reactivation of the enzyme by 2-mercaptoethanol was prevented if the enzyme-oADP complex was previously reduced by NaBH₄, suggesting that the reaction product was a stable Schiff's base. Protection from inactivation was afforded by nucleotides (NAD⁺, NADH and ADP) demonstrating the specificity of the reaction. When the enzyme was completely inactivated, approx. 1 mol of [14C]oADP per mol. of subunit was incorporated. Cleavage of [14C]oADP-modified enzyme with trypsin and subsequent sepn. of peptides by RP-HPLC gave only one radioactive peak. Amino-acid sequencing of the radioactive tryptic peptide revealed the target site of oADP reaction to be Lys360. These results indicate that oADP inactivates FDH by specific reaction at the nucleotide binding site, with neg. cooperativity between subunits accounting for the appearance of two phases of inactivation. Mol. modeling studies were used to create a model of *C. boidinii* FDH, based on the known structure of the *Pseudomonas* enzyme, using the MODELLER 4 program. The model confirmed that Lys360 is positioned at the NAD⁺-binding site. Site-directed mutagenesis was used in dissecting the structure and functional role of Lys360. The mutant Lys360.fwdarw.Ala enzyme exhibited unchanged k_{cat} and K_m values for formate but showed reduced affinity for NAD⁺. The mol. model was used to help interpret these biochem. data concerning the Lys360.fwdarw.Ala

enzyme. The data are discussed in terms of engineering coenzyme specificity.

REFERENCE 2: 128:318376 Periodate-oxidized ATP stimulates the permeability transition of rat liver mitochondria. Henke, Wolfgang; Hagen, Thilo; Jung, Klaus; Loening, Stefan A. (University Hospital Charite, Department of Urology, Research Division, Humboldt University, Berlin, D-10098, Germany). *Biochimica et Biophysica Acta*, 1363(3), 209-216 (English) 1998. CODEN: BBACAQ. ISSN: 0006-3002. Publisher: Elsevier Science B.V..

AB Periodate-oxidized ADP (oADP) and periodate-oxidized ATP (oATP) stimulate the permeability transition in energized rat liver mitochondria measured as the Ca^{2+} -efflux induced by Ca^{2+} and P_i . In the presence of Mg^{2+} and P_i , mitochondria lose intramitochondrial adenine nucleotides at a slow rate. oATP induces a strong decrease of the matrix adenine nucleotides which is inhibited by carboxyatractyloside. Under these conditions, Mg^{2+} prevents the opening of the permeability transition pore. EGTA prevents the P_i -induced slow efflux of adenine nucleotides, but is without effect on the oATP-induced strong decrease of adenine nucleotides. This oATP-induced strong adenine nucleotide efflux is inhibited by ADP. oATP reduces the increase of matrix adenine nucleotides occurring when the mitochondria are incubated with Mg^{2+} and ATP. This effect of oATP is also prevented by carboxyatractyloside. oATP is not taken up by the mitochondria. It is suggested that oATP induces a strong efflux of matrix adenine nucleotides by the interaction with the ADP/ATP carrier from the cytosolic side. The induction of the mitochondrial permeability transition by oADP and oATP is attributed to two mechanisms-a strong decrease in the intramitochondrial adenine nucleotide content, esp. that of ADP, and a stabilization of the c-conformation of the ADP/ATP carrier.

REFERENCE 3: 111:111566 Studies on the active site of the *Neurospora crassa* plasma membrane hydrogen ion ATPase with periodate-oxidized nucleotides. Bidwai, Ashok P.; Morjana, Nihmat A.; Scarborough, Gene A. (Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27599, USA). *J. Biol. Chem.*, 264(20), 11790-5 (English) 1989. CODEN: JBCHA3. ISSN: 0021-9258.

AB The *N. crassa* plasma membrane H^{+} -ATPase is inactivated by the periodate-oxidized nucleotides, oATP, oADP, and oAMP, (o indicates the oxidized form of the nucleotide) with oAMP the most effective. Inhibition of the ATPase is essentially irreversible, because Sephadex G-50 column chromatog. of the oAMP-treated ATPase does not result in a reversal of the inhibition. Inhibition of the ATPase by oAMP is protected against by the H^{+} -ATPase substrate ATP, the product ADP, and the competitive inhibitors TNP [2',3'-O-(2,4,6-trinitrocyclohexadienylidene)-ATP and TNP-ADP, suggesting that oAMP inhibition occurs at the nucleotide binding site of the enzyme. The rate of inactivation of the ATPase by oAMP is only slightly affected by EDTA, indicating the the oAMP interaction with the nucleotide binding site of the H^{+} -ATPase occurs in the absence of a divalent cation. The protection against oAMP inhibition by ADP is likewise unaffected by EDTA. The inhibition of the ATPase by oAMP is absolutely dependent on the presence of acidic phospholipids or acidic lysophospholipids known to be required for H^{+} -ATPase activity, suggesting that these lipids either aid in the formation of the nucleotide binding site or render it accessible. Incubation of the ATPase with Mg^{2+} plus vanadate, which locks the enzyme in a conformation resembling the transition state of the enzyme dephosphorylation reaction, completely protects against inhibition by oAMP, suggesting that in this transition state conformation the nucleotide site either does not exist, or is inaccessible to oAMP. Labeling studies with [^{14}C]oAMP indicate that the incorporation of 1 mol of oAMP is sufficient to cause complete inactivation of the ATPase.

REFERENCE 4: 108:109991 Identification of high-affinity (K_d 0.35 $\mu\text{mol/L}$) and low-affinity (K_d 7.9 $\mu\text{mol/L}$) platelet binding sites for ADP and

competition by ADP analogs. Jefferson, John R.; Harmon, Joan T.; Jamieson, G. A. (Am. Red. Cross Cell Biol. Lab., Rockville, MD, USA). Blood, 71(1), 110-16 (English) 1988. CODEN: BLOOAW. ISSN: 0006-4971.

- AB Steady-state binding of ADP to paraformaldehyde-fixed human blood platelets was studied. The results (1) provide accurate parameters for the binding of ADP to fixed platelets in the absence of complications due to metab. and secretion, (2) demonstrate that both high-affinity ($K_d = 0.35 \mu\text{M}$) and low-affinity ($K_d = 7.9 \mu\text{M}$) binding sites are present and that both are accessible to ADP and C-2-substituted ADP analogs, and (3) suggest that the high-affinity binding site corresponds to the receptor modulating platelet activation by ADP. These results help to define possible platelet receptors for ADP and may provide a useful indicator system for evaluating the interaction of agonists and antagonists with platelets.

REFERENCE 5: 108:37111 Electrostatic interactions between organic ions. Part 2. Phosphates with amines. Wilson, Henry R.; Williams, Robert J. P. (Inorg. Chem. Lab., Oxford, OX1 3QR, UK). J. Chem. Soc., Faraday Trans. 1, 83(6), 1885-92 (English) 1987. CODEN: JCFTAR. ISSN: 0300-9599.

- AB Assocn. consts. of org. cations with org. phosphate anions have been detd. using an NMR procedure. The consts. are compared with expectation based on the Bjerrum theory of ion-pair formation. The values of the consts. are rather different from those for simple and complex inorg. ions with the same org. phosphates. The importance of the difference for biol. systems is stressed.

REFERENCE 6: 106:171905 Isolation and sequence determination of an active site peptide of rabbit muscle pyruvate kinase. Bezares, Guillermo; Eyzaguirre, Jaime; Hinrichs, Maria Victoria; Heinrikson, Robert L.; Reardon, Ilene; Kemp, Robert G.; Latshaw, Steven P.; Bazaes, Sergio (Lab. Bioquim., Univ. Catol. Chile, Santiago, Chile). Arch. Biochem. Biophys., 253(1), 133-7 (English) 1987. CODEN: ABBIA4. ISSN: 0003-9861.

- AB Rabbit muscle pyruvate kinase was inactivated by 2',3'-dialdehyde ADP with the incorporation of reagent/enzyme subunit. The inactivated protein was digested with trypsin after reduct. and carboxymethylation. The labeled peptide was isolated by gel filtration and further purified by HPLC. The peptide was sequenced both by liq.-phase and gas-phase automatic edman degradn. A 34-residue peptide was obtained. This peptide is identical to a tryptic peptide labeled with trinitrobenzenesulfonate from bovine muscle pyruvate kinase. Available evidence suggests that dialdehyde ADP labels the enzyme at the same lysine in position 2 of the peptide. The high homol. between the isolated peptide and regions of other pyruvate kinases from low-to-high eukaryotes supports the idea that this peptide is related to the enzyme active site.

REFERENCE 7: 105:56934 Pyruvate kinase: studies on affinity labeling and active-site structure using the rabbit muscle enzyme. Eyzaguirre, Jaime; Bazaes, Sergio; Bezares, Guillermo; Hinrichs, Maria Victoria; Heinrikson, Robert L.; Reardon, Ilene (Lab. Bioquim., Univ. Catol. Chile, Chile). Arch. Biol. Med. Exp., 18(3-4), 317-23 (English) 1985. CODEN: ABMXA2. ISSN: 0004-0533.

- AB The dialdehyde-ADP affinity-labeled active site peptide of rabbit muscle pyruvate kinase has sequence homol. with yeast and bovine and chicken muscle kinases. Based on this homol., the affinity-labeled active site residue is tentatively identified as lysine-25. Affinity labeling inactivation kinetics, active site residues and domain localization, and other structural features of the rabbit muscle kinase are reviewed.

REFERENCE 8: 104:84140 Affinity modification of creatine kinase and ATP-ADP translocase in heart mitochondria: determination of their molar stoichiometry. Kuznetsov, A. V.; Saks, V. A. (Lab. Bioenerg., Res. Cent. Cardiol., Moscow, 121552, USSR). Biochem. Biophys. Res. Commun., 134(1),

359-66 (English) 1986. CODEN: BBRCA9. ISSN: 0006-291X.

- AB Oxidized dialdehyde analogs of ADP or ATP (oADP and oATP, resp.) irreversibly inhibited adenine nucleotide translocator (T) and creatine kinase (CK) in heart mitochondria. Inactivation of T and CK was parallel with carboxyatractyloside (CAT)-sensitive and (ADP-plus-phosphocreatine)-sensitive incorporation of o[3H]ADP into mitochondria, resp. The o[3H]ADP incorporation sensitive to CAT or ADP-plus-phosphocreatine was used to det. T and CK contents, resp., in mitochondria. T content in cardiac mitochondria from rat, rabbit, dog, and chicken was 2.6-2.9 mol/mol cytochrome aa3. The same T/cytochrome aa3 ratio was found in liver mitochondria with lower cytochrome aa3 content. In all types of cardiac mitochondria, CK content was 2.4-2.6 mol/mol cytochrome aa3. Thus, T and CK are present in a molar ratio of 1:1 in all types of cardiac mitochondria.

REFERENCE 9: 103:209690 Dialdehyde derivatives of purine mononucleotides: substrate properties and affinity modification of myosin ATPase. Grishin, M. N.; Kodentsova, V. M.; Abdraimova, U. A.; Nikolaeva, O. P.; Petushkova, E. V. (Dep. Biochem., Moscow State Univ., Moscow, USSR). Biokhimiya (Moscow), 50(9), 1517-22 (Russian) 1985. CODEN: BIOHAO. ISSN: 0006-307X.

- AB The dialdehyde deriv. of ATP (oxo-ATP) is a good substrate for the Ca-ATPase of heavy meromyosin [$K_m = (1.2-1.4) \cdot 10^{-4} M$; $V = V$ for ATP]. At the same time, this compd. can irreversibly inhibit the enzyme. Since oxo-ATP is rapidly hydrolyzed by myosin to form oxo-ADP, this inhibition is the result of the enzyme interaction with oxo-ADP. The kinetics of heavy meromyosin inhibition by oxo-ADP are typical of affinity modification; in this case, ATP fully protects heavy meromyosin from the activity loss. Similar results on the irreversible inhibition of the ATPase by oxo-ADP were obtained in the presence of myosin, heavy meromyosin, myosin subfragment-1, and natural actomyosin and in the absence of divalent cations, thus suggesting the modification of the active center of myosin ATPase.

REFERENCE 10: 103:85120 Inhibition of membrane-bound chloroplast coupling factor 1 by a dephosphorylated derivative of dialdehyde ADP. Garbarino, Joan E.; Jagendorf, Andre T. (Plant Biol. Sect., Cornell Univ., Ithaca, NY, 14853, USA). J. Biol. Chem., 260(14), 8297-300 (English) 1985. CODEN: JBCHA3. ISSN: 0021-9258.

- AB Periodate-oxidized ADP, if left in aq. soln., loses its phosphates by β -elimination. This dephosphorylated dialdehyde compd. caused rapid and irreversible inhibition of membrane-bound spinach chloroplast coupling factor 1 (CF1). Inhibition was 2.5 times faster in the light than in the dark. A high concn. of uncoupler eliminated the light stimulation. Light could be replaced by an acid-base transition. Therefore, the dialdehyde reacts with a site or sites on CF1 that become exposed by a high-energy state-induced conformational change. The substrate nucleotides ADP, ATP, GDP, and GTP protected against inhibition, whereas Pi and the nonsubstrate nucleotides AMP, GMP, CTP, and UTP did not. The protection by GTP was competitive and Mg-dependent, suggesting that the dialdehyde binds to a nucleotide-binding site. However, the corresponding UDP and CDP dialdehyde derivs. also inhibited CF1 and showed the light-stimulation effect, indicating that the adenine is not important for the binding. These derivs. could be binding to a nucleotide-binding site or to another reactive site that becomes exposed during the light-induced conformational change. In the latter case the protection by substrate nucleotides would be due to prevention of the energy-dependent conformational change.

L13 ANSWER 146 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 63713-53-1 REGISTRY

CN Hexanedioic acid, dihydrazide, polymer with [R-(R*,R*)]-P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] triphosphate (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

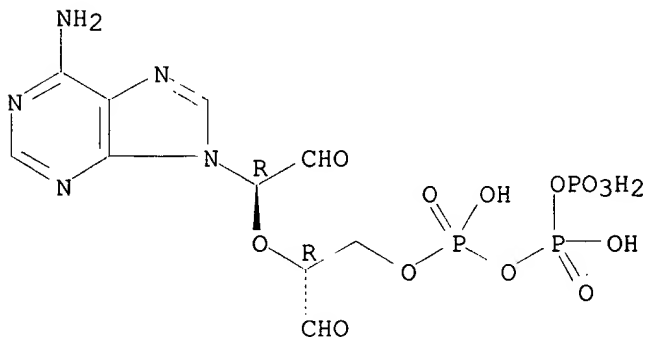
CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [R-(R*,R*)]-, polymer with hexanedioic acid dihydrazide (9CI)
 FS STEREOSEARCH
 MF (C10 H14 N5 O13 P3 . C6 H14 N4 O2)x
 CI PMS
 PCT Polyamine, Polyazomethine, Polyazomethine formed, Polyether, Polyother
 LC STN Files: CA, CAPLUS

CM 1

CRN 54970-91-1

CMF C10 H14 N5 O13 P3

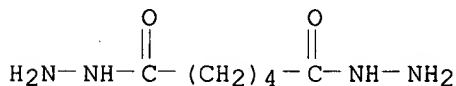
Absolute stereochemistry.



CM 2

CRN 1071-93-8

CMF C6 H14 N4 O2



1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 87:34682 Interaction of adipic acid dihydrazide analog of ATP with myosin. Involvement of the essential sulfhydryl groups. Reisler, Emil; Lamed, Raphael (Polym. Dep., Weizmann Inst. Sci., Rehovot, Israel). Biochemistry, 16(11), 2532-8 (English) 1977. CODEN: BICHAW.

AB The hydrolysis by myosin of a sol. ATP analog, adipic acid dihydrazide-ATP (I), proceeds in a fashion similar to the hydrolysis of ATP by myosin modified at either of the 2 essential SH groups. In both systems, the Mg2+-activated hydrolysis of the nucleotide is increased, whereas the EDTA-stimulated activity is inhibited. Blocking of SH1 or SH2 leads to a complete inhibition of I hydrolysis. I is unable to expose the SH2 for modification by thiol reagents. Apparently, I need interact with only 1 of the 2 essential thiol sites of myosin. The hydrolysis of Mg-I by myosin is inhibited by a large excess of actin and does not result in contraction of actomyosin threads. Mg-I is also a rather weak dissociation agent of the acto-heavy meromyosin complex. These properties of I are discussed in conjunction with modification studies of myosin and the

mechanism of ATP hydrolysis.

L13 ANSWER 147 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 58176-57-1 REGISTRY

CN Diphosphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, [S-(R*,S*)]-

OTHER NAMES:

CN ADP 2',3'-dialcohol

CN orADP

CN rro-ADP

CN rroADP

FS STEREOSEARCH

DR 61504-13-0

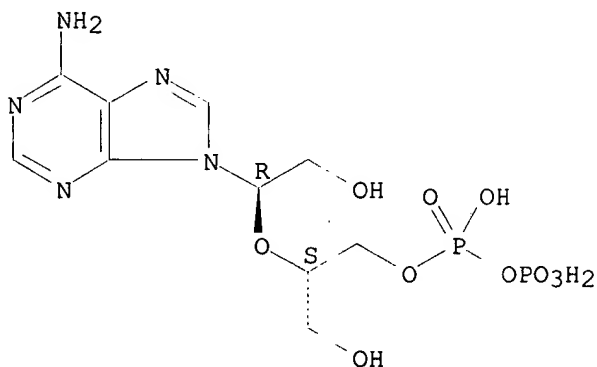
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CI COM

LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1967 TO DATE)

10 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 102:42017 Some properties of the nucleotide-binding site of troponin T kinase-casein kinase type II from skeletal muscle. Risnik, V. V.; Gusev, N. B. (Sch. Biol., Moscow State Univ., Moscow, 119899, USSR). Biochim. Biophys. Acta, 790(2), 108-16 (English) 1984. CODEN: BBACAQ. ISSN: 0006-3002.

AB Investigation of properties of skeletal muscle troponin T kinase (EC 2.7.1.37) revealed that the enzyme belongs to the group of type II casein kinases. The enzyme consists of 2 subunits with apparent mol. wts. of 44,000 and 26,000 and contains a protein with mol. wt. of 39,000, which is probably the proteolytic fragment of the 44,000-mol.-wt. subunit. The substrate specificity of troponin T kinase was tested, using 20 nucleotide analogs. The enzyme has a low substrate specificity toward the purine base and uses both ATP and GTP as substrates. Modification of the ribose ring does not influence the enzyme interaction with the nucleotide; however, the cleavage of ribose leads to a decrease of the enzyme-nucleotide interaction. Elimination of the .gamma.-terminal

Searched by: Mary Hale 308-4258 CM-1 12D16

phosphate or its modification by bulky hydrophobic radicals do not affect this interaction. A comparison of the K_i values for different analogs suggests that the interaction of troponin T kinase with the nucleotide occurs via the binding of the purine base and the .beta.-phosphate group of the analog.

REFERENCE 2: 98:89799 Borohydride reduction of periodate-oxidized nucleotides; isolation and structure of the reduction intermediate. Rosenthal, Luann P.; Hogenkamp, Harry P. C.; Bodley, James W. (Dep. Biochem., Univ. Minnesota, Minneapolis, MN, 55455, USA). Carbohydr. Res., 111(1), 85-91 (English) 1982. CODEN: CRBRAT. ISSN: 0008-6215.

AB The redn. of periodate-oxidized nucleotides with NaBH_4 proceeds via a reaction intermediate presumed to be a monoalc. The borohydride-redn. intermediate of periodate-oxidized ADP has been isolated by anion-exchange, liq. chromatog., and subjected to redn. Redn. by NaBH_4 and NaBD_4 showed that the 2 aldehyde groups are sequentially reduced in the order 3' and 2', and that the isolated intermediate corresponds to the semi-reduced, 3'-alc., 2'-aldehyde deriv. This compd. is a useful analog for the study of enzymes and proteins that interact with nucleotides.

REFERENCE 3: 95:183043 Photophosphorylation of ribose modified ADP analogs by spinach chloroplasts. Boos, K. S.; Dimke, B.; Schlimme, E.; Wiedner, H.; Edelman, K.; Strotmann, H. (Lab. Biol. Chem., Univ. Paderborn, Paderborn, 4790, Fed. Rep. Ger.). FEBS Lett., 130(1), 73-6 (English) 1981. CODEN: FEBLAL. ISSN: 0014-5793.

AB The ADP-binding site of chloroplast ATP synthase (I) was mapped by use of ribose-modified ADP analogs. Neither the C2' nor the C3' hydroxyl group was essential for ADP binding and phosphorylation. The results suggested that free rotation of the base around the N-glycosidic linkage as well as rotation around the C4'-C5' bond and pseudorotation of the ribose ring are essential features of the nucleotide mol. with regard to recognition and catalysis by the I active site.

REFERENCE 4: 90:201339 Factors influencing the response of human blood platelets to analogs of ADP which may act as partial agonists at the ADP receptor. Egan, Christopher M.; Fisher, Antony P.; Scrutton, Michael C. (Dep. Biochem., Univ. London, London, Engl.). Eur. J. Biochem., 95(1), 127-37 (English) 1979. CODEN: EJBICAI. ISSN: 0014-2956.

AB The prior addn. of nonaggregating concns. of the divalent cation ionophore A-23187 caused human platelets to aggregate in response to a subsequent addn. of the 2'3'-dialdehyde and 2',3'-dialc. derivs. of ADP (oADP and orADP, resp.), which act as partial agonists at the platelet ADP receptor inducing only the transition from discoid to globular morphol. (shape change). A secretion response was also obsd. on addn. of a low concn. of ionophore A-23187 prior to orADP. These responses were not obsd. if ionophore A-23187 was added prior to the 2',3'-dialdehyde and 2',3'-dialc. derivs. of ATP (oATP and orATP, resp) and were markedly inhibited by prior addn. of the ADP antagonist adenosine 5'-[.beta.,.gamma.-methylene]triphosphate. The aggregation response to oADP in the presence of ionophore A-23187 was reduced but not eliminated by addn. of 3 mM EGTA when studies were performed in heparinized platelet-rich plasma. Addns. of 3 mM EGTA in citrated platelet-rich plasma or 4 mM EDTA in either system completely inhibited this response. Inhibitors which were reported to elevate the intracellular concn. of cyclic AMP or to prevent Ca^{2+} movement also inhibited the aggregation response to oADP which was obsd. in the presence of ionophore A-23187. Prior addn. of inhibitors of adenylate cyclase failed to cause an aggregation response to subsequent addn. of oADP or orADP. Certain of these inhibitors enhanced and prolonged the shape change response to oADP or orADP but only at concns. an order of magnitude in excess of those required to antagonize inhibition by agents such as PGE_1 , which act by increasing the concn. of cyclic AMP. The concn. of PGE_1 , adenosine, or papaverine required to inhibit shape

change induced by oADP was 1-2 orders of magnitude lower than that required to inhibit shape change induced by ADP. Prior addn. of oADP decreased the lag phase in the response of human platelets to arachidonate while also increasing the concn. required to observe half-maximal response and causing a decrease in the extent of that response. Prior addn. of oATP also diminished the extent of this response and increased the concn. of arachidonate required but had no effect on the lag phase. Evidently, oADP and orADP are capable only of acting as partial agonists at the ADP receptor because of a defective ability to increase cytosolic Ca^{2+} concn. This defect is rectified by the presence of low concns. of ionophore A-23187, which promotes mobilization of Ca^{2+} from an intracellular store. The results do not appear consistent with the thesis that a decrease in platelet cyclic AMP is an initiating event in aggregation induced by ADP, but do support a model which implicates cyclic AMP in depletion of cytosolic Ca^{2+} .

REFERENCE 5: 90:35503 Activity of polynucleotide phosphorylase with nucleoside diphosphates containing sugar ring modifications. Hawley, D. M.; Sninsky, J. J.; Bennett, G. N.; Gilham, P. T. (Dep. Biol. Sci., Purdue Univ., West Lafayette, Indiana, USA). *Biochemistry*, 17(11), 2082-6 (English) 1978. CODEN: BICHAW. ISSN: 0006-2960.

AB A no. of nucleoside 5'-diphosphates contg. modifications in their sugar rings were synthesized, and the capacity of these nucleotides to act as substrates for polynucleotide phosphorylase was examd. The 5'-diphosphates of 9- β -D-arabinofuranosyladenine (ara-A) and 3'-deoxyadenosine were prepd. by phosphorylation of the nucleosides with POC13 followed by condensation of the resulting 5'-phosphates with inorg. phosphate using 1,1'-carbonyldiimidazole as the activating agent. The 5'-diphosphate of each ox-red nucleoside (a nucleoside in the the C2'-C3' bond has been cleaved) was synthesized by oxidn. of the 2',3'-cis-diol groups in the 5'-diphosphates of adenosine, cytidine, guanosine, and uridine with NaIO_4 followed by the redn. of the resulting dialdehydes with NaBH_4 . Similar conditions were also used to prep. the ox-red nucleosides as well as their 5'-phosphates and 5'-triphosphates. In a study of the capacity of modified nucleotides to add to a small oligoribonucleotide in the presence of polynucleotide phosphorylase, 2 classes of activity were exhibited: (1) the addn. of a few residues of the nucleotide as in the case of the diphosphates of ara-A, 2'-deoxynucleosides, and (under certain conditions) 2'-O-(α -methoxyethyl)nucleosides; (2) the addn. of only 1 nucleotide residue as in the case of the diphosphates of the ox-red nucleosides and 3'-deoxyadenosine. The activity displayed by the latter class may be of value as a method for the radioactive labeling of the 3'-terminal ends of polyribonucleotides and RNA.

REFERENCE 6: 89:160853 Interaction of human blood platelets with the 2',3'-dialdehyde and 2',3'-dialcohol derivatives of adenosine 5'-diphosphate and adenosine 5'-triphosphate. Pearce, P. Helen; Wright, Judith M.; Egan, Christopher M.; Scrutton, Michael C. (Dep. Biochem., Univ. London King's Coll., London, Engl.). *Eur. J. Biochem.*, 88(2), 543-54 (English) 1978. CODEN: EJBCAI. ISSN: 0014-2956.

AB The 2',3'-dialdehyde deriv. of ADP (oADP) at concns. approaching the millimolar range induces human blood platelets to undergo shape change, but is incapable of inducing aggregation. When incubated with platelets for 1 min before addn. of the agonist, oADP acts as a competitive inhibitor of shape change and aggregation induced by ADP. Under these conditions secretion and hence aggregation induced by low concns. of collagen, and secretion and hence secondary aggregation induced by adrenaline, thrombin and vasopressin are also inhibited by this analog. In addn., oADP stimulates the rate of primary aggregation induced by adrenaline and causes partial inhibition of primary aggregation induced by thrombin or vasopressin. When longer preincubation times are employed the extent of inhibition with respect to all agonists, except for high concns.

of collagen, is increased and the competitive character of the inhibition with respect to ADP is no longer apparent. Incubation of human platelets with the 2',3'-dialdehyde deriv. of ATP (oATP) causes effects similar to those for oADP except that the analog neither induces platelet shape change, nor stimulates the rate of primary aggregation induced by adrenaline. In addn. oATP fails to cause significant inhibition of platelet shape change induced by serotonin. The inhibition caused by oATP is not a function of the time of incubation. The 2',3'-dialc. derivs. of ADP and ATP (orADP and orATP) effect the aggregation properties of human blood platelets in a manner generally resembling those obsd. for the 2',3'-dialdehyde analogs. However, orADP is only weakly effective in causing platelet shape change and stimulating the rate of primary aggregation induced by adrenaline and does not inhibit secretion induced by adrenaline, collagen, thrombin, and vasopressin. The inhibition by orADP increases only slightly with increased time of incubation. Apparently, oADP acts as a partial agonist, whereas oATP and orADP as antagonists for the platelet ADP receptor.

REFERENCE 7: 89:125139 The requirements of cis-diol grouping and riboside structure in adenine-containing drugs for the inhibitory action on the activity of rat myocardial protein kinase. Hynie, Sixtus; Smrt, Jiri (Fac. Med., Charles Univ., Prague, Czech.). Collect. Czech. Chem. Commun., 43(6), 1531-7 (English) 1978. CODEN: CCCCAK. ISSN: 0366-547X.

AB The influence of OH group masking in adenosine and its nucleotides on the activity of rat myocardial protein kinase was studied by measuring the incorporation of 32P from ATP-32P into histones. Compared with the inhibitory effect of AMP, ADP, and ATP, the adenosine nucleotide 2',3'-O-ethoxymethylene derivs. inhibited incorporation only weakly. Acyclic 9-[1',5'-dihydroxy-4'(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]adenine 5'-diphosphate had no effect on kinase activity. The active site of protein kinase apparently requires both OH groups and a rigid configuration in the ribose moiety.

REFERENCE 8: 89:39574 Studies on the tight adenine nucleotide binding site of chloroplast coupling factor (CF1). Strotmann, H.; Bickel-Sandkoetter, S.; Edelmann, K.; Schlimme, E.; Boos, K. S.; Luestorff, J. (Bot. Inst., Tieraerztl. Hochsch. Hannover, Hannover, Ger.). BBA Libr., 14(Struct. Funct. Energy-Transducing Membr.), 307-17 (English) 1977. CODEN: BBALAJ. ISSN: 0067-2734.

AB A study of the specificities of 14 different ADP analogs in light-induced incorporation into membrane-bound chloroplast coupling factor (CF1), using 3-times-washed broken chloroplasts of spinach, indicated that the structural features of the ADP mol. required in the process of ATP formation are entirely different from those which are relevant in tight binding by CF1. In tight binding there was a high specificity for the adenine base, suggesting that the base moiety is the recognition site of the nucleotide mol. In the process of photophosphorylation, base specificity is different from that obtained in binding to CF1. Replacement of the amino group at C-6 by O (IDP, GDP) had a comparatively small effect on phosphorylation. In contrast, altering the N-1 of the heterocyclic ring (ADP-1-oxide, 1-amino- IDP) decreased the specificity to a much greater extent. In tight binding as well as in phosphorylation, anti-conformation of the adenine base relative to the sugar moiety appears to be required.

REFERENCE 9: 84:105964 Oligonucleotidic compounds. LVII. Free-conformational analogs of nucleotides and oligonucleotides derived from 9-[1',5'-dihydroxy-4'(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]adenine. Smrt, J.; Mikhailov, S. N.; Hynie, S.; Florent'ev, V. L. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, Czech.). Collect. Czech. Chem. Commun., 40(11), 3399-403 (English) 1975. CODEN: CCCCAK.

GI For diagram(s), see printed CA Issue.

AB AMP was transformed by NaIO₄ oxidn. and NaBH₄ redn. into 9-[1',5'-dihydroxy-4'(S)-hydroxymethyl-3'-oxapent-2'-(R)-yl]adenine 5'-phosphate (I). ADP, adenylyl-(3'.fwdarw.5')-adenosine, and uridylyl-(3'.fwdarw.5')-adenylyl-(3'.fwdarw.5')-adenosine were transformed analogously. With N,N'-dicyclohexylcarbodiimide, I gave 9-[1',5'-dihydroxy-4'-(1''-hydroxymethyl)-3'-oxapent-2'(R)-yl]adenine 5',1''-cyclic phosphate. 9-[1',5'-Dihydroxy-4'(S)-hydroxymethyl-3'-oxapent-2'-(R)-yl]adenine 5'-diphosphate inhibited the polymn. of ADP with polynucleotide phosphorylase.

REFERENCE 10: 84:55397 Properties of the ribose-ring-opened adenine nucleotide 2,2'-[1-(9-adenyl)-1'-(tri-, diphosphoryloxymethyl)]dihydroxydiethyl ether in mitochondrial adenine nucleotide translocation. Boos, Karl S.; Schlimme, Eckhard; Bojanovski, Dubo; Lamprecht, Walther (Inst. Klin. Biochem. Physiol. Chem., Med. Hochsch. Hannover, Hannover, Ger.). Eur. J. Biochem., 60(2), 451-8 (English) 1975. CODEN: EJBACI.

AB 14C- or 32P-labeled 2,2'[1-(9-adenyl)-1'-(tri-, diphosphoryloxymethyl)]dihydroxydiethyl ether (rroANP) was obtained from ANP by cleavage of the C-2'-C-3' bond by Na periodate oxidn. and subsequent borohydride redn. Binding of rroANP to rat liver mitochondria revealed carrier-linked atractyloside-sensitive and nonspecific atractyloside-insensitive binding but no transfer across the inner mitochondrial membrane. Kinetic data indicated rroANP as a competitive inhibitor for ANP uptake with K_i = 9.3 .times. 10⁻⁵ M. Exptl. rroANP confirmed that an intact adenine base and 3 anionic charges of the phosphate chain are essential for the recognition between ANP-carrier and nucleotide but unsufficient for the induction of a transmembrane ANP exchange. In addn., mobilization of the carrier-nucleotide complex required an intact ribofuranoside ring system.

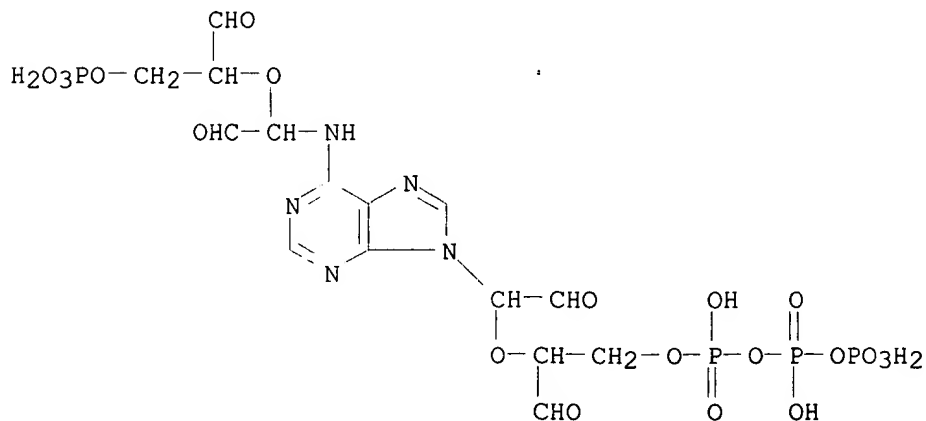
L13 ANSWER 148 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 56475-05-9 REGISTRY

CN Triphosphoric acid, P-[2-[1-[6-[1-[1-formyl-2-(phosphonooxy)ethoxy]-2-oxoethyl]amino]-9H-purin-9-yl]-2-oxoethoxy]-3-oxopropyl] ester, stereoisomer (9CI) (CA INDEX NAME)

MF C15 H21 N5 O20 P4

LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

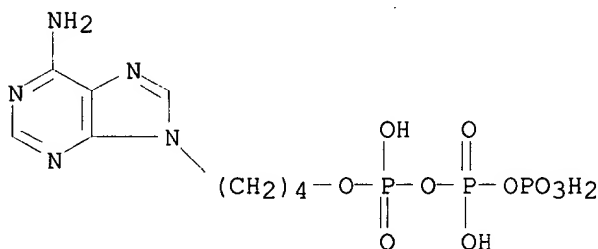
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

REFERENCE 1: 83:93004 Stereochemical course of the adenosine triphosphate phosphoribosyltransferase reaction in histidine biosynthesis. Chelsky, Daniel; Parsons, Stanley M. (Dep. Chem., Univ. California, Santa Barbara, Calif., USA). J. Biol. Chem., 250(14), 5669-73 (English) 1975. CODEN: JBCHA3.

AB The product of the 1st reaction in histidine biosynthesis was shown by optical rotation measurements on 3 derivs. to have inverted, .beta. stereochem. at the newly formed bond. This is in contrast to .alpha. linkage expected on the basis of previously obsd. exchange, specificity, and covalent intermediate phenomena. The postulated double displacement mechanism for ATP phosphoribosyltransferase (EC 2.4.2.17) must be modified to account for the product stereochem.

L13 ANSWER 149 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 55881-02-2 REGISTRY
 CN Triphosphoric acid, P-[4-(6-amino-9H-purin-9-yl)butyl] ester (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C9 H16 N5 O10 P3
 CI COM.
 LC STN Files: BEILSTEIN*, CA, CAPLUS
 (*File contains numerically searchable property data)



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5 REFERENCES IN FILE CA (1967 TO DATE)
 5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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AB Triphosphoalkyladenines ppp(CH₂)_nA (I; n = 2-4) and the ATP deriv. (II) inhibited RNA elongation competitively with respect to all 4 natural nucleoside triphosphates, whereas 3'-O-methyl-ATP (III) was a competitive inhibitor only with respect to ATP. I and II were not incorporated into RNA; III was, terminating elongation. The mol. wt. distribution of nascent RNA transcripts of a phage T7 template in the presence of I or II was the same as the normal distribution due to pauses in elongation. This suggests that I and II act by prolonging the natural pauses in RNA formation. This suggestion is supported by the fact that I (n = 3) reduces the rate of chain termination by 3'-O-methyl-GTP. The kinetics of inhibition by I resembled inhibition by inorg. pyrophosphate, which suggests that they interact weakly and reversibly with the substrate-binding site of RNA polymerase.

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Searched by: Mary Hale 308-4258 CM-1 12D16

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- AB The parameters of the hydrolysis of ATP and several analogs by sol. mitochondrial ATPase (I) were detd. The V_{max} of the reaction decreased as follows: 2'-deoxy-ATP > ATP > etheno-ATP > GTP > 3'-O-methyl-ATP > UTP. ATP, 2'-deoxy-ATP, 3'-O-methyl-ATP, GTP, and etheno-ATP were hydrolyzed by I with similar apparent K_m values. CTP was not hydrolyzed by I and did not inhibit the I reaction at a concn. of 10-2M. Nucleoside triphosphate derivs. with an open ribose ring, 9-[1',5'-dihydroxy-4'-(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]adenine-5'-triphosphate and 1-[1',5'-dihydroxy-4'-(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]cytosine-5'-triphosphate, were effective inhibitors of ATPase (K_i .apprx.5 .times. 10^{-5} M). I bound ATP analogs having hydrocarbon radicals, $(CH_2)_2$, $(CH_2)_3$, and $(CH_2)_4$, instead of the ribose residues. 9-(3'-Hydroxypropyl)-adenine-3'-triphosphate and 9-(4-hydroxybutyl)adenine-4'-triphosphate were not hydrolyzed by I, although they inhibited the I reaction ($K_i = 2$.times. 10^{-4} M). 9-(2'-Hydroxyethyl)adenine-2'-triphosphate was hydrolyzed by I 8-fold more slowly than ATP. It is suggested that the hydrolysis of substrates of I is preceded by the binding of the substrates in a strained conformation in the active site.

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- AB Various nonglycosidic analogs of ATP were weak inhibitors of transcription in vitro, competing with ATP for the RNA polymerase binding site. Only 3'-O-methyl-ATP (but not 2'-O-methyl-ATP) was an effective inhibitor, causing irreversible inhibition of RNA synthesis at ionic strength 0.13 and 25.degree.. This was apparently due to its incorporation into the terminal position of the growing RNA chain. However, at increased temp. and ionic strength, 3'-O-methyl-ATP became a reversible competitive inhibitor with a K_i of 4 .times. 10^{-5} M. The mechanism of inhibition was discussed.

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Kritsyn, A. M.; Mikhailov, S. M.; Kolobushkina, L. I.; Padyukova, N. Sh.; Florent'ev, V. L. (Inst. Mol. Biol., Moscow, USSR). Izv. Akad. Nauk SSSR, Ser. Khim. (8), 1846-50 (Russian) 1975. CODEN: IASKA6.

GI For diagram(s), see printed CA Issue.

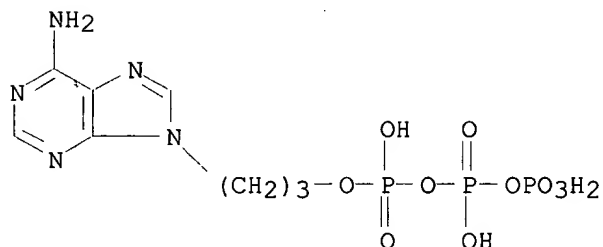
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- AB The response was studied of the title reaction catalyzed by the enzyme from bovine pancreas to adenine and adenosine and their 9-hydroxyalkylated analogs and their triphosphates and ATP with a 3'-O-Me block. Adenine and adenosine and their hydroxyalkyl analogs and triphosphates were competitive inhibitors of ATP in the pyrophosphate exchange reaction. Adenosine had inhibitory activity similar to that of ATP; the others were

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L13 ANSWER 150 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 55881-01-1 REGISTRY
 CN Triphosphoric acid, P-[3-(6-amino-9H-purin-9-yl)propyl] ester (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C8 H14 N5 O10 P3
 CI COM
 LC STN Files: BEILSTEIN*, CA, CAPLUS
 (*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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Searched by: Mary Hale 308-4258 CM-1 12D16

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GI For diagram(s), see printed CA Issue.

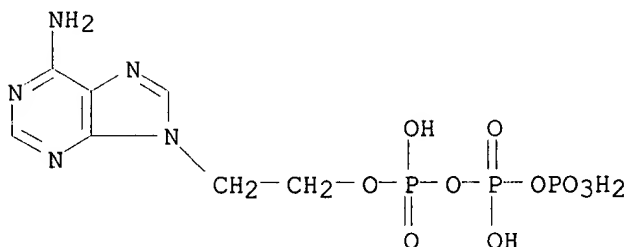
AB Monophosphates I, II, III [R = P(O)(OH)₂, n = 2, 3, 4] were obtained in 48-94% yields by phosphorylation of the corresponding alc. with cyanoethyl phosphate in the presence of N,N'-dicyclohexylcarbodiimide. Triphosphates I [R = P(O)(OH)OP(O)(OH)OP(O)(OH)₂, n = 4] and III [R = P(O)(OH)OP(O)(OH)OP(O)(OH)₂, n = 2, 3, 4] were obtained in 59-68% yields by phosphorylation of salts of the monophosphates with bis(tert-butylammonium) pyrophosphate.

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L13 ANSWER 151 OF 166 REGISTRY COPYRIGHT 2002 ACS
RN 55881-00-0 REGISTRY
CN Triphosphoric acid, P-[2-(6-amino-9H-purin-9-yl)ethyl] ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C7 H12 N5 O10 P3
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:13062 Inhibitory effect on HT-1080 tumor cell invasion in vitro using 9-(2'-hydroxyethyl)adenine 2'-phosphates. Kitade, Yukio; Hayashi, Masa-Atsu; Yatome, Chizuko; Chajima, Masamitsu; Nagase, Hisamitsu (Laboratory of Molecular Biochemistry, Department of Chemistry, Faculty of Engineering, Gifu University, Gifu, 501-11, Japan). Bioorganic & Medicinal Chemistry Letters, 7(7), 833-836 (English) 1997. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier.

AB Several 9-(2'-hydroxyethyl)purine 2'-phosphates shoed a moderate inhibitory effect of tumor cell invasion using Matrigel. These 2'-phosphates also inhibited the activity on type IV collagen degrdn. by matrix metalloprotease-9.

REFERENCE 2: 106:63465 Nucleoside 5'-triphosphates modified at sugar residues as substrates for calf thymus terminal deoxynucleotidyl transferase and for AMV reverse transcriptase. Bibilashvilli, R. S.; Skamrov, A. V.; Kutateladze, T. V.; Mazo, A. M.; Kraevskii, A. A.; Kukhanova, M. K. (Natl. Cardiol. Res. Cent., Moscow, USSR). Biochim. Biophys. Acta, 868(2-3), 136-44 (English) 1986. CODEN: BBACAQ. ISSN: 0006-3002.

AB Terminal deoxynucleotidyltransferase from calf thymus and AMV (avian myeloblastosis virus) RNA-directed DNA polymerase (reverse transcriptase) catalyze the incorporation of 3'-amino-2',3'-dideoxynucleoside 5'-triphosphates, as well as some of their 3'-derivs., e.g., 3'-amino-3'-deoxyarabinonucleoside 5'-triphosphates, and some other nucleoside 5'-triphosphates modified at sugar residues. After incorporation of the appropriate 5'-mononucleotide residue into the DNA, further chain elongation is blocked. This finding opens up the possibility of selective inhibition of DNA synthesis catalyzed by a certain enzyme.

Searched by: Mary Hale 308-4258 CM-1 12D16

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GI For diagram(s), see printed CA Issue.

AB Monophosphates I, II, III [R = P(O)(OH)₂, n = 2, 3, 4] were obtained in 48-94% yields by phosphorylation of the corresponding alc. with cyanoethyl phosphate in the presence of N,N'-dicyclohexylcarbodiimide. Triphosphates I [R = P(O)(OH)OP(O)(OH)OP(O)(OH)₂, n = 4] and III [R = P(O)(OH)OP(O)(OH)OP(O)(OH)₂, n = 2, 3, 4] were obtained in 59-68% yields by phosphorylation of salts of the monophosphates with bis(tert-butylammonium) pyrophosphate.

REFERENCE 7: 83:39358 Effect of 9-(ω -hydroxyalkyl)adenines and their triphosphates on the ATP-[32P]-pyrophosphate exchange reaction catalyzed by tryptophanyl tRNA synthetase. Prasolov, V. S.; Kritsyn, A. M.; Mikhailov, S. N.; Florent'ev, V. L. (Inst. Mol. Biol., Moscow, USSR). Dokl. Akad. Nauk SSSR, 221(5), 1226-8 [Biochem] (Russian) 1975. CODEN: DANKAS.

AB The response was studied of the title reaction catalyzed by the enzyme from bovine pancreas to adenine and adenosine and their 9-hydroxyalkylated analogs and their triphosphates and ATP with a 3'-O-Me block. Adenine and adenosine and their hydroxyalkyl analogs and triphosphates were competitive inhibitors of ATP in the pyrophosphate exchange reaction. Adenosine had inhibitory activity similar to that of ATP; the others were an order of magnitude less effective. Introducing a 2nd OH into the alkyl chain lowered the activity to that of adenosine itself. Tests of S- and racemic forms of the 9-(2,3-dihydroxypropyl)adenine showed that the configuration at the 2'-C is immaterial for binding the inhibitor to the active site. Inhibition by 3'-O-Me-ATP was noncompetitive. The ATPase mol. may have sites other than the ATP-binding site which interact with adenosine nucleotides. Evidence was found for esp. high activity of the 3'-OH group for ATP binding to the active site.

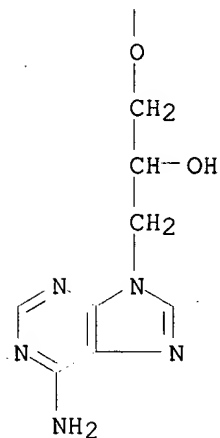
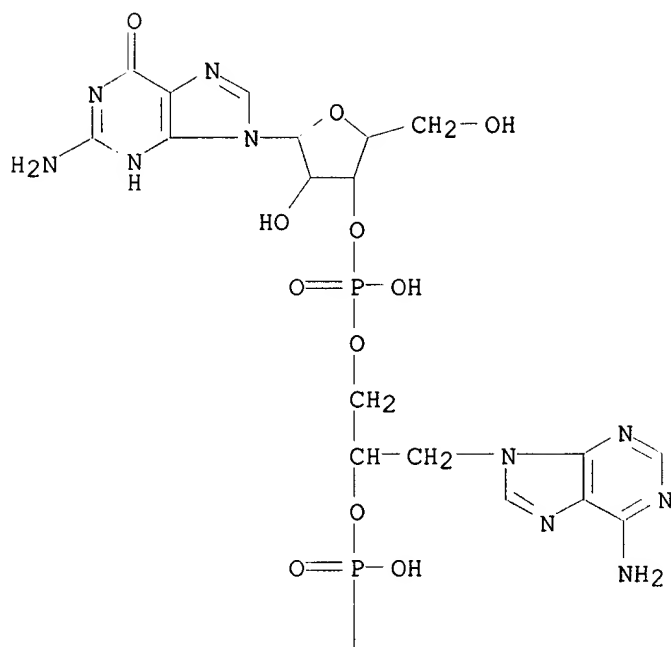
L13 ANSWER 152 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 55559-96-1 REGISTRY

CN 3'-Guanylic acid, mono[3-(6-amino-9H-purin-9-yl)-2-[[[3-(6-amino-9H-purin-9-yl)-2-hydroxypropoxy]hydroxyphosphinyl]oxy]propyl] ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

MF C26 H33 N15 O13 P2

LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

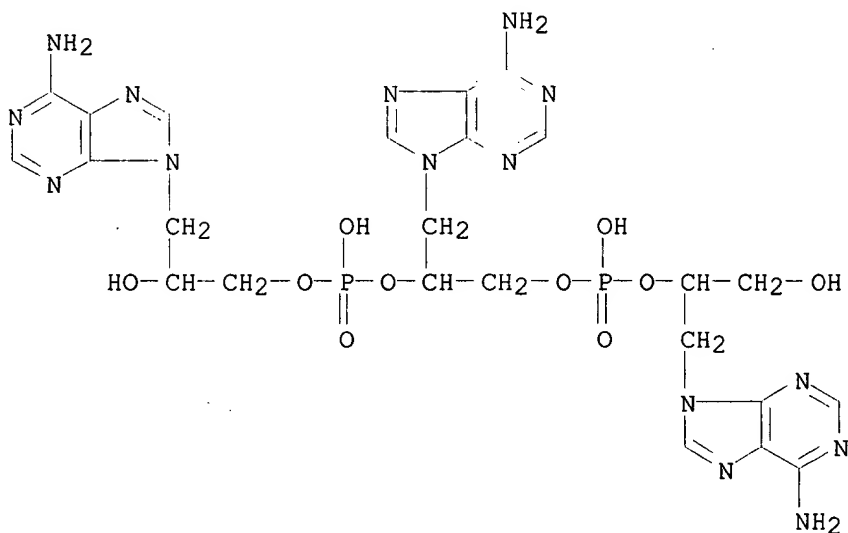
REFERENCE 1: 82:171341 Nucleic acid components and their analogs. CLXXII.
Aliphatic analogs of nucleosides, nucleotides, and oligonucleotides.
Holy, A. (Inst. Org. Chem. Biochem., Czech. Acad Sci., Prague, Czech.).
Collect. Czech. Chem. Commun., 40(1), 187-214 (English) 1975. CODEN:
CCCCAK.

AB Condensation of thymine Na salt (I) with 1-O-p-toluenesulfonyl-2,3-O-

Searched by: Mary Hale 308-4258 CM-1 12D16

isopropylidene-D-glycerol in DMF at 100.degree. and hydrolysis in refluxing 80% aq. AcOH gave a mixt. of (S)-1-(2,3-dihydroxypropyl)thymine and (S)-3-(2,3-dihydroxypropyl)thymine. The corresponding (R) enantiomers were prepd. by condensation of I with Me 5-O-p-toluenesulfonyl-2,3-O-isopropylidene-D-ribofuranoside, removal of the Me2C: group, NaIO4 oxidn., and NaBH4 redn. (RS)-1-(3,4-Dihydroxybutyl)thymine was prepd. from 1,2-O-isopropylidene-4-p-toluenesulfonyl-1,2,4-butanetriol. Condensation of N6,O2'-Diacetyl-(S)-(2,3-dihydroxypropyl)adenine 3'-phosphate with 3'-O-triphenylmethyl-(S)-9-(2,3-dihydroxypropyl) adenine and deblocking gave the ApA analog, (S)-9-(2,3-dihydroxypropyl)adenine-2'-phosphoryl-3'-(S)-9-(2,3- dihydroxypropyl)adenine. Repetition of this process gave the ApApA analog (S)-9-(2,3-dihydroxypropyl)adenine-2'-phosphoryl-3'-(S)-9-(2,3- dihydroxypropyl)-adenine-2'-phosphoryl-3'-(S)-9-(2,3-dihydroxypropyl) adenine (II). (S)-9-(2,3-Dihydroxypropyl)adenine-2'-O-phosphoryl-5'-adenosine and adeny-3'-yl-3-(S)-9-(2,3-dihydroxypropyl)adenine were also prepd. II and analogs of GpUpU, GpCpU, and GpApA triplets did not stimulate the aminoacyl-tRNA bond to ribosomes.

L13 ANSWER 153 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 55559-89-2 REGISTRY
 CN Phosphoric acid, mono[3-(6-amino-9H-purin-9-yl)-2-[[[3-(6-amino-9H-purin-9-yl)-2-hydroxypropoxy]hydroxyphosphinyl]oxy]propyl] mono[2-(6-amino-9H-purin-9-yl)-1-(hydroxymethyl)ethyl] ester, stereoisomer (9CI) (CA INDEX NAME)
 MF C24 H31 N15 O10 P2
 LC STN Files: BEILSTEIN*, CA, CAPLUS
 (*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 82:171341 Nucleic acid components and their analogs. CLXXII. Aliphatic analogs of nucleosides, nucleotides, and oligonucleotides. Holy, A. (Inst. Org. Chem. Biochem., Czech. Acad Sci., Prague, Czech.). Collect. Czech. Chem. Commun., 40(1), 187-214 (English) 1975. CODEN: CCCCAK.

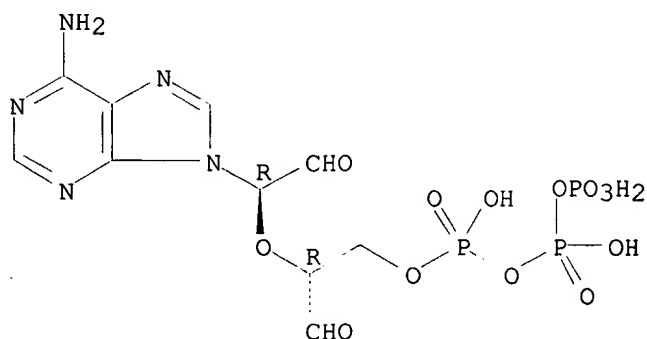
AB Condensation of thymine Na salt (I) with 1-O-p-toluenesulfonyl-2,3-O-

Searched by: Mary Hale 308-4258 CM-1 12D16

isopropylidene-D-glycerol in DMF at 100.degree. and hydrolysis in refluxing 80% aq. AcOH gave a mixt. of (S)-1-(2,3-dihydroxypropyl)thymine and (S)-3-(2,3-dihydroxypropyl)thymine. The corresponding (R) enantiomers were prepd. by condensation of I with Me 5-O-p-toluenesulfonyl-2,3-O-isopropylidene-D-ribofuranoside, removal of the Me2C: group, NaIO4 oxidn., and NaBH4 redn. (RS)-1-(3,4-Dihydroxybutyl)thymine was prepd. from 1,2-O-isopropylidene-4-p-toluenesulfonyl-1,2,4-butanetriol. Condensation of N6,O2'-Diacetyl-(S)-(2,3-dihydroxypropyl)adenine 3'-phosphate with 3'-O-triphenylmethyl-(S)-9-(2,3-dihydroxypropyl)adenine and deblocking gave the ApA analog, (S)-9-(2,3-dihydroxypropyl)adenine-2'-phosphoryl-3'-(S)-9-(2,3-dihydroxypropyl)adenine. Repetition of this process gave the ApApA analog (S)-9-(2,3-dihydroxypropyl)adenine-2'-phosphoryl-3'-(S)-9-(2,3-dihydroxypropyl)-adenine-2'-phosphoryl-3'-(S)-9-(2,3-dihydroxypropyl)adenine (II). (S)-9-(2,3-Dihydroxypropyl)adenine-2'-O-phosphoryl-5'-adenosine and adenylyl-3'-yl-3-(S)-9-(2,3-dihydroxypropyl)adenine were also prepd. II and analogs of GpUpU, GpCpU, and GpApA triplets did not stimulate the aminoacyl-tRNA bond to ribosomes.

L13 ANSWER 154 OF 166 REGISTRY COPYRIGHT 2002 ACS
 RN 54970-91-1 REGISTRY
 CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [R-(R*,R*)]-
 OTHER NAMES:
 CN 2',3'-dialdehyde ATP
 CN Adenosine 5'-triphosphate dialdehyde
 CN ATP 2',3'-dialdehyde
 CN oATP
 CN ro-ATP
 CN roATP
 FS STEREOSEARCH
 MF C10 H14 N5 O13 P3
 CI COM
 LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, EMBASE, MEDLINE, TOXCENTER, USPATFULL
 (*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

82 REFERENCES IN FILE CA (1967 TO DATE)
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

Searched by: Mary Hale 308-4258 CM-1 12D16

82 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:161360 Adenosine-5'-triphosphate-2',3'-dialdehyde as antiinflammatory medicament. Ferrero, Maria Elena (Universita' Degli Studi di Milano, Italy). PCT Int. Appl. WO 2002011737 A2 20020214, 13 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-EP8643 20010726. PRIORITY: IT 2000-MI1827 20000804.

AB The use of adenosine-5'-triphosphate-2',3'-dialdehyde as a medicament useful for the treatment of inflammatory conditions is disclosed.

REFERENCE 2: 134:320660 The influence of mechlorethamine on the activity of ecto-ATPase of rat lymphocytes. Purzyc, L.; Calkosinski, I. (Dep. Biochemistry, Fr.). Annales Pharmaceutiques Francaises, 59(1), 33-39 (English) 2001. CODEN: APFRAD. ISSN: 0003-4509. Publisher: Masson Editeur.

AB Mechlorethamine, is an immunomodulator widely used in therapy although its effect on plasma membrane - bound enzymes is unclear. In rats with an inflammatory state, an increased activity of ecto-ATPase was obsd. both in the B and T subpopulations of lymphocytes. A single administration of mechlorethamine (simultaneously with carrageenin - inflammation factor), either in immunomodulating (5.mu.g/kg) or cytotoxic (600.mu.g/kg) dose, decrease the enzymic activity in both subpopulations but to higher degree in the case of cytotoxic dose. In in vitro studies, after administering mechlorethamine, a diminution of inhibiting potential of the inhibitors blocking the nucleophilic site of proteins was noticed. This confirms the hypothesis that mechlorethamine attacks the catalytic part of the ecto-enzyme contg. a nucleophilic group. Classical inhibitors of apyrase, -Hg2+, c-erythrosin B and suramine - did not cause any significant change in the activity of ecto-ATPase, what confirms the fact that these enzymes belong to different groups.

REFERENCE 3: 134:202973 The P2 purinergic receptors of human dendritic cells: identification and coupling to cytokine release. Ferrari, Davide; La Sala, Andrea; Chiozzi, Paola; Morelli, Anna; Falzoni, Simonetta; Girolomoni, Giampiero; Idzko, Marco; Dichmann, Stefan; Norgauer, Johannes; Di Virgilio, Francesco (Department of Experimental and Diagnostic Medicine, Section of General Pathology, University of Ferrara, Ferrara, I-44100, Italy). FASEB Journal, 14(15), 2466-2476 (English) 2000. CODEN: FAJOEC. ISSN: 0892-6638. Publisher: Federation of American Societies for Experimental Biology.

AB The authors investigated the expression of purinoceptors in human dendritic cells, providing functional, pharmacol., and biochem. evidence that immature and mature cells express P2Y and P2X subtypes, coupled to increase in the intracellular Ca2+, membrane depolarization, and secretion of inflammatory cytokines. The ATP-activated Ca2+ change was biphasic, with a fast release from intracellular stores and a delayed influx across the plasma membrane. A prolonged exposure to ATP was toxic to dendritic cells that swelled, lost typical dendrites, became phase lucent, detached from the substrate, and eventually died. These changes were highly suggestive of expression of the cytotoxic receptor P2X7, as confirmed by ability of dendritic cells to become permeant to membrane impermeant dyes such as Lucifer yellow or ethidium bromide. The P2X7 receptor ligand 2',3'-(4-benzoyl-benzoyl)-ATP was a better agonist than ATP for Ca2+ increase and plasma membrane depolarization. Oxidized ATP, a covalent blocker of P2X receptors, and the selective P2X7 antagonist KN-62

inhibited both permeabilization and Ca^{2+} changes induced by ATP. The following purinoceptors were expressed by immature and mature dendritic cells: P2Y1, P2Y2, P2Y5, P2Y11 and P2X1, P2X4, P2X7. Finally, stimulation of LPS-matured cells with ATP triggered release of IL-1 β and TNF- α . Purinoceptors may provide a new avenue to modulation of dendritic cells function.

- REFERENCE 4: 132:344793 Capping DNA with DNA. Li, Yingfu; Liu, Yong; Breaker, Ronald R. (Department of Molecular Cellular and Developmental Biology, Yale University, New Haven, CT, 06520-8103, USA). *Biochemistry*, 39(11), 3106-3114 (English) 2000. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.
- AB Twelve classes of deoxyribozymes that promote an ATP-dependent "self-capping" reaction were isolated by in vitro selection from a random-sequence pool of DNA. Each deoxyribozyme catalyzes the transfer of the AMP moiety of ATP to its 5'-terminal phosphate group, thereby forming a 5',5'-pyrophosphate linkage. An identical DNA adenylate structure is generated by the T4 DNA ligase during enzymic DNA ligation. A 41-nucleotide class 1 deoxyribozyme requires Cu^{2+} as a cofactor and adopts a structure that recognizes both the adenine and triphosphate moieties of ATP or dATP. The catalytic efficiency for this DNA, measured at 104 M-1.cntdot.min-1 using either ATP or dATP as substrate, is similar to other catalytic nucleic acids that use small substrates. Chem. probing and site-directed mutagenesis implicate the formation of guanine quartets as crit. components of the active structure. The observation of ATP-dependent "self-charging" by DNA suggests that DNA could be made to perform the reactions typically assocd. with DNA cloning, but without the assistance of protein enzymes.
- REFERENCE 5: 131:308295 Metal-dependent nucleotide binding to the Escherichia coli rotamase SlyD. Mitterauer, Thomas; Nanoff, Christian; Ahorn, Horst; Freissmuth, Michael; Hohenegger, Martin (Institute of Pharmacology, University of Vienna, Vienna, A-1090, Austria). *Biochemical Journal*, 342(1), 33-39 (English) 1999. CODEN: BIJOAK. ISSN: 0264-6021. Publisher: Portland Press Ltd..
- AB Upon expression and purifn. of the first catalytic domain of mammalian adenylate cyclase type 1 (IC1), a 27 kDa contaminant was obsd., which was labeled by three radioactive ATP analogs (8-azido-ATP, 3'-O-(4-benzoyl)benzoyl-ATP and 2',3'-dialdehyde-ATP); the protein was purified sep. and identified as Escherichia coli SlyD by N-terminal amino acid sequence detn. SlyD is the host protein required for lysis of E. coli upon infection with bacteriophage .PHI.X174 and has recently been shown to display rotamase (peptidylproline cis-trans-isomerase) activity. The covalent incorporation of ATP analogs into SlyD was promoted by bivalent transition metal ions (Zn^{2+} .gtoreq. Ni^{2+} > Co^{2+} > Cu^{2+}) but not by Mg^{2+} or Ca^{2+} ; this is consistent with the known metal ion specificity of SlyD. ATP, ADP, GTP and UTP suppressed labeling of SlyD with comparable potencies. Similarly, SlyD bound 2',3'-O-(2,4,6-trinitrophenyl)-ATP with an affinity in the range of 10 .mu.M, as detd. by fluorescence enhancement. This interaction was further augmented in the presence of Zn^{2+} (K_d = .apprx.2.mu.M at satg. Zn^{2+}) but not of Mg^{2+} . Irresp. of the assay conditions, hydrolysis of nucleotides by SlyD was not detected. Upon gel filtration on a Superose HR 12 column, SlyD (predicted mol. mass = 21 kDa) migrated with an apparent mol. mass of 44 kDa, indicating that the protein was a dimer. However, the migration of SlyD was not affected by the presence of Zn^{2+} or of Zn^{2+} and ATP. Thus we concluded that SlyD binds nucleotides in the presence of metal ions. These findings suggest that SlyD serves a physiol. role that goes beyond that accounted for by its intrinsic rotamase activity, which is obsd. in the absence of metal ions.

REFERENCE 6: 131:141359 Kinetic Characterization of a T-State of Ascaris

suum Phosphofructokinase with Heterotropic Negative Cooperativity by ATP Eliminated. Jagannatha Rao, G. S.; Cook, Paul F.; Harris, Ben G. (Department of Molecular Biology and Immunology, University of North Texas Health Science Center at Fort Worth, Fort Worth, TX, 76107, USA). Archives of Biochemistry and Biophysics, 365(2), 335-343 (English) 1999. CODEN: ABBIA4. ISSN: 0003-9861. Publisher: Academic Press.

- AB The affinity analog, 2',3'-dialdehyde ATP has been used to chem. modify the ATP-inhibitory site of *Ascaris suum* phosphofructokinase, thereby locking the enzyme into a less active T-state. This enzyme form has a max. velocity that is 10% that of the native enzyme in the direction of fructose 6-phosphate (F6P) phosphorylation. The enzyme displays sigmoidal satn. for the substrate fructose 6-phosphate ($S_{0.5}$ (F6P) = 19 mM and n_H = 2.2) at pH 6.8 and a hyperbolic satn. curve for MgATP with a K_m identical to that for the native enzyme. The allosteric effectors, fructose 2,6-bisphosphate and AMP, do not affect the $S_{0.5}$ for F6P but produce a slight (1.5- and 2-fold, resp.) V-type activation with K_a values (effector concn. required for half-maximal activation) of 0.40 and 0.24 mM, resp. Their activating effects are additive and not synergistic. The kinetic mechanism for the modified enzyme is steady-state-ordered with MgATP as the first substrate and MgADP as the last product to be released from the enzyme surface. The decrease in V and V/K values for the reactants likely results from a decrease in the equil. const. for the isomerization of the E:MgATP binary complex, thus favoring an unisomerized form. The V and $V/KF6P$ are pH dependent with similar pK values of about 7 on the acid side and 9.8 on the basic side. The microenvironment of the active site appears to be affected minimally as evidenced by the similarity of the pK values for the groups involved in the binding site for F6P in the modified and native enzymes. (c) 1999 Academic Press.

REFERENCE 7: 131:2065 Covalent modification of Lys19 in the CTP binding site of cytidine 5'-monophosphate N-acetylneuraminic acid synthetase. Tullius, Michael V.; Vann, Willie F.; Gibson, Bradford W. (Department of Pharmaceutical Chemistry, University of California, San Francisco, CA, 94143-0446, USA). Protein Science, 8(3), 666-675 (English) 1999. CODEN: PRCIEI. ISSN: 0961-8368. Publisher: Cambridge University Press.

- AB Periodate oxidized CTP (oCTP) was used to investigate the importance of lysine residues in the CTP binding site of the CMP N-acetylneuraminic acid (CMP-NeuAc) synthetase (EC 2.7.7.43) from *Haemophilus ducreyi*. The reaction of oCTP with the enzyme follows pseudo-first-order satn. kinetics, giving a max. rate of inactivation of 0.6 min⁻¹ and a K_I of 6.0 mM at pH 7.1. Mass spectrometric anal. of the modified enzyme provided data that was consistent with .beta.-elimination of triphosphate after the reaction of oCTP with the enzyme. A fully reduced enzyme-oCTP conjugate, retaining the triphosphate moiety, was obtained by inclusion of NaBH₃CN in the reaction soln. The .beta.-elimination product of oCTP reacted several times more rapidly with the enzyme compared to equiv. concns. of oCTP. This compd. also formed a stable reduced morpholino adduct with CMP-NeuAc synthetase when the reaction was conducted in the presence of NaBH₃CN, and was found to be a useful lysine modifying reagent. The substrate CTP was capable of protecting the enzyme to a large degree from inactivation by oCTP and its .beta.-elimination product. Lys19, a residue conserved in CMP-NeuAc synthetases, was identified as being labeled with the .beta.-elimination product of oCTP.

REFERENCE 8: 128:318376 Periodate-oxidized ATP stimulates the permeability transition of rat liver mitochondria. Henke, Wolfgang; Hagen, Thilo; Jung, Klaus; Loening, Stefan A. (University Hospital Charite, Department of Urology, Research Division, Humboldt University, Berlin, D-10098, Germany). Biochimica et Biophysica Acta, 1363(3), 209-216 (English) 1998. CODEN: BBACAQ. ISSN: 0006-3002. Publisher: Elsevier Science B.V..

- AB Periodate-oxidized ADP (oADP) and periodate-oxidized ATP (oATP) stimulate the permeability transition in energized rat liver mitochondria measured

as the Ca^{2+} -efflux induced by Ca^{2+} and Pi . In the presence of Mg^{2+} and Pi , mitochondria lose intramitochondrial adenine nucleotides at a slow rate. oATP induces a strong decrease of the matrix adenine nucleotides which is inhibited by carboxyatractyloside. Under these conditions, Mg^{2+} prevents the opening of the permeability transition pore. EGTA prevents the Pi -induced slow efflux of adenine nucleotides, but is without effect on the oATP-induced strong decrease of adenine nucleotides. This oATP-induced strong adenine nucleotide efflux is inhibited by ADP. oATP reduces the increase of matrix adenine nucleotides occurring when the mitochondria are incubated with Mg^{2+} and ATP. This effect of oATP is also prevented by carboxyatractyloside. oATP is not taken up by the mitochondria. It is suggested that oATP induces a strong efflux of matrix adenine nucleotides by the interaction with the ADP/ATP carrier from the cytosolic side. The induction of the mitochondrial permeability transition by oADP and oATP is attributed to two mechanisms-a strong decrease in the intramitochondrial adenine nucleotide content, esp. that of ADP, and a stabilization of the c-conformation of the ADP/ATP carrier.

- REFERENCE 9: 123:187708 Potentiating and inhibitory effects of periodate-oxidized ATP analogs on contractions of vas deferens to ATP. Fedan, Jeffrey S.; Grant, L. Jameel R. (Physiology Section, Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, 1095 Willowdale Road, Morgantown, WV, 26505, USA). Eur. J. Pharmacol., 281(2), 213-17 (English) 1995. CODEN: EJPHAZ. ISSN: 0014-2999.
- AB Previous studies have shown that treatment of guinea-pig isolated vas deferens with the affinity label periodate-oxidized ATP (2',3'-dialdehyde ATP), results in two irreversible effects on biphasic contractile responses to ATP, i.e., potentiation of the P2X purinoceptor-mediated first phase and inhibition of the ecto-kinase-mediated second phase. The present expts. were designed to evaluate whether periodate-oxidized ADP, periodate-oxidized AMP, and periodate-oxidized adenosine, produce similar effects. Periodate-oxidized ATP and periodate-oxidized ADP (10-2 M) elicited contraction of the vas deferens (periodate-oxidized ATP > periodate-oxidized ADP); periodate-oxidized AMP and periodate-oxidized adenosine had no agonist activity. After incubation of the preps. for 5 min with 10-2 M periodate-oxidized ATP, periodate-oxidized ADP, periodate-oxidized AMP or periodate-oxidized adenosine, the first phase of contraction to submaximal ATP concns. was potentiated. Simultaneously, periodate-oxidized ATP, periodate-oxidized ADP and periodate-oxidized AMP inhibited the second contractile phase, whereas periodate-oxidized adenosine did not. The results indicate that the requirement for 5'-phosphate to produce potentiation and inhibition is different: 5'-phosphate is not needed to potentiate the first phase of contraction to ATP, but at least one 5'-phosphate is required to inhibit the second phase of contraction.
- REFERENCE 10: 123:106093 Nucleotide binding by the HIV-1 integrase protein in vitro. Lipford, J. Russell; Worland, Stephen T.; Farnet, Chris M. (Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA). J. Acquired Immune Defic. Syndr., 7(12), 1215-23 (English) 1994. CODEN: JAISSET. ISSN: 0894-9255.
- AB Recombinant human immunodeficiency virus type 1 (HIV-1) integrase was shown to bind ATP and other nucleoside triphosphates and nucleotide analogs in vitro. Crosslinking of ATP and the photoaffinity analog 8-azido-ATP to integrase occurred in a UV dose-dependent manner. Covalent binding of ATP to integrase was also achieved without UV irradiation when the nucleotide was oxidized to the 2',3'-dialdehyde deriv. (oxidized ATP) prior to incubation with the protein, indicating the presence of a reactive lysine residue in the nucleotide binding region of the protein. A no. of exptl. observations indicate that nucleotides and DNA substrates bind at the same or overlapping site(s) on the integrase protein. For

example, the binding of nucleotides or nucleotide analogs to integrase was blocked by prior incubation with DNA substrates, and the covalent crosslinking of 8-azido-ATP to integrase inhibited the DNA binding and oligonucleotide cleavage activities of the protein. Oxidized ATP inhibited the oligonucleotide cleavage activity of integrase at concns. that had no effect on DNA binding, suggesting that oxidized nucleotides may specifically target the catalytic center of the enzyme. These studies indicate that nucleotide analogs may serve as probes for the DNA binding and catalytic sites of the enzyme and may serve as models for the design of active site inhibitors of retroviral integrase.

L13 ANSWER 155 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 42248-41-9 REGISTRY

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[6-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahex-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[6-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-2,4-dioxo-1,3-diphosphahex-1-yl]-.beta.-D-ribofuranosyl]-, inner salt, P,P'-dioxide

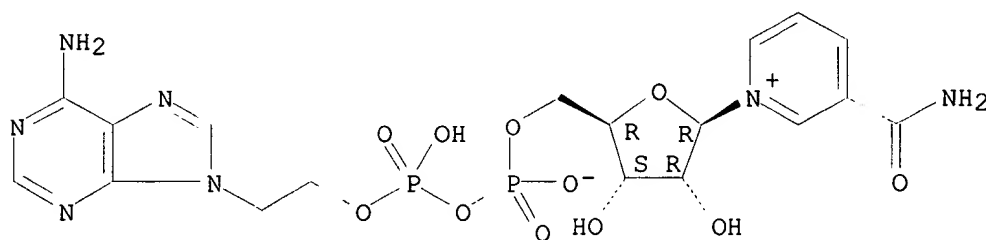
FS STEREOSEARCH

MF C18 H23 N7 O11 P2

LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 79:32239 Interactions of the nonfunctional coenzyme binding site in dehydrogenases with [nicotinamide-ribofuranosyl]-[.omega.-(adenin-9-yl)-n-alkyl] pyrophosphates. Jeck, Reinhard; Wilhelm, Gabriele (Chem.-Physiol. Inst., Univ. Frankfurt, Frankfurt/M., Ger.). Justus Liebigs Ann. Chem. (3), 531-43 (German) 1973. CODEN: JLACBF.

GI For diagram(s), see printed CA Issue.

AB The NAD analogs I (n = 2-5) were prepd. by condensation of .omega.-(adenin-9-yl)alkyl pyrophosphate with NMN. I and their enzymically prepd. dihydro derivs. (II) had nearly identical chem. and phys. properties with NAD+ and NADH, resp. I and II were active as H acceptors or H donors, resp., with alc. dehydrogenase (E.C. 1.1.1.1) (III) from yeast or horse liver, lactate dehydrogenase (E.C. 1.1.1.27), or cytoplasmic or mitochondrial malate dehydrogenase (E.C. 1.1.1.37). I and II showed high Michaelis consts. compared to NAD+ and NADH, but lower (except with III of horse liver) catalytic consts.

L13 ANSWER 156 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 42188-29-4 REGISTRY

CN 3-Pyridinecarboxamide, 1-[5-O-[9-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphanon-1-yl]-.beta.-D-ribofuranosyl]-1,4-dihydro- (9CI) (CA INDEX NAME)

Searched by: Mary Hale 308-4258 CM-1 12D16

OTHER CA INDEX NAMES:

CN Diphosphoric acid, P-[5-(6-amino-9H-purin-9-yl)pentyl] ester, P'.fwdarw.5' ester with 1,4-dihydro-1-.beta.-D-ribofuranosyl-3-pyridinecarboxamide

OTHER NAMES:

CN 3-Pyridinecarboxamide, 1-[5-O-[[[[[5-(6-amino-9H-purin-9-yl)pentyl]oxy]hydroxyphosphinyl]oxy]hydroxyphosphinyl]-.beta.-D-ribofuranosyl]-1,4-dihydro-

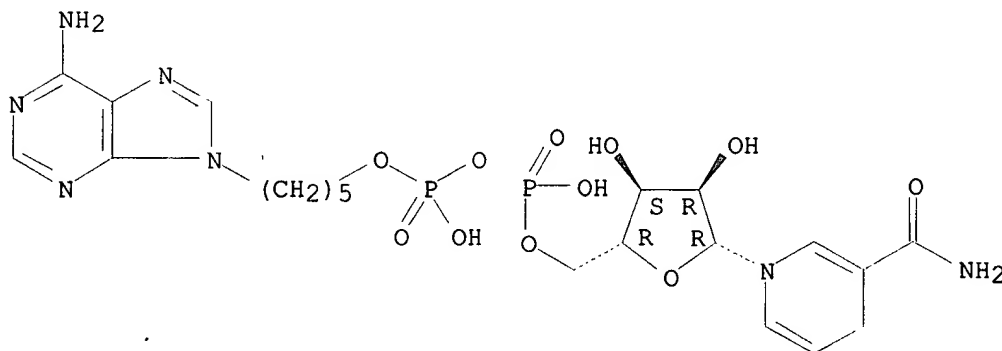
FS STEREOSEARCH

MF C21 H31 N7 O11 P2

LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 79:32239 Interactions of the nonfunctional coenzyme binding site in dehydrogenases with [nicotinamide-ribofuranosyl]-[.omega.-(adenin-9-yl)-n-alkyl] pyrophosphates. Jeck, Reinhard; Wilhelm, Gabriele (Chem.-Physiol. Inst., Univ. Frankfurt, Frankfurt/M., Ger.). Justus Liebigs Ann. Chem. (3), 531-43 (German) 1973. CODEN: JLACBF.

GI For diagram(s), see printed CA Issue.

AB The NAD analogs I (n = 2-5) were prepd. by condensation of .omega.-(adenin-9-yl)alkyl pyrophosphate with NMN. I and their enzymically prepd. dihydro derivs. (II) had nearly identical chem. and phys. properties with NAD+ and NADH, resp. I and II were active as H acceptors or H donors, resp., with alc. dehydrogenase (E.C. 1.1.1.1) (III) from yeast or horse liver, lactate dehydrogenase (E.C. 1.1.1.27), or cytoplasmic or mitochondrial malate dehydrogenase (E.C. 1.1.1.37). I and II showed high Michaelis consts. compared to NAD+ and NADH, but lower (except with III of horse liver) catalytic consts.

L13 ANSWER 157 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 42188-28-3 REGISTRY

CN 3-Pyridinecarboxamide, 1-[5-O-[8-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphaoct-1-yl]-.beta.-D-ribofuranosyl]-1,4-dihydro- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

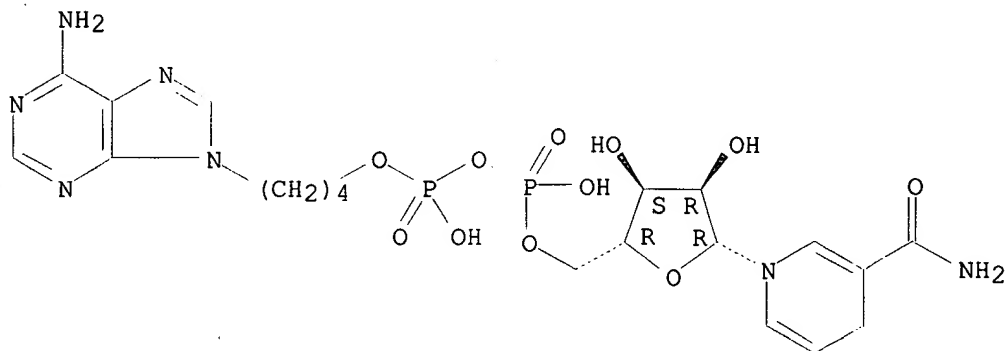
CN Diphosphoric acid, P-[4-(6-amino-9H-purin-9-yl)butyl] ester, P'.fwdarw.5'-ester with 1,4-dihydro-1-.beta.-D-ribofuranosyl-3-pyridinecarboxamide

Searched by: Mary Hale 308-4258 CM-1 12D16

OTHER NAMES:

CN 3-Pyridinecarboxamide, 1-[5-O-[[[[[4-(6-amino-9H-purin-9-yl)butyl]oxy]hydroxyphosphinyl]oxy]hydroxyphosphinyl]-.beta.-D-ribofuranosyl]-1,4-dihydro-
 FS STEREOSEARCH
 MF C20 H29 N7 O11 P2
 LC STN Files: BEILSTEIN*, CA, CAPLUS
 (*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 79:32239 Interactions of the nonfunctional coenzyme binding site in dehydrogenases with [nicotinamide-ribofuranosyl]-[.omega.-(adenin-9-yl)-n-alkyl] pyrophosphates. Jeck, Reinhard; Wilhelm, Gabriele (Chem.-Physiol. Inst., Univ. Frankfurt, Frankfurt/M., Ger.). Justus Liebigs Ann. Chem. (3), 531-43 (German) 1973. CODEN: JLACBF.

GI For diagram(s), see printed CA Issue.

AB The NAD analogs I (n = 2-5) were prepd. by condensation of .omega.-(adenin-9-yl)alkyl pyrophosphate with NMN. I and their enzymically prepd. dihydro derivs. (II) had nearly identical chem. and phys. properties with NAD+ and NADH, resp. I and II were active as H acceptors or H donors, resp., with alc. dehydrogenase (E.C. 1.1.1.1) (III) from yeast or horse liver, lactate dehydrogenase (E.C. 1.1.1.27), or cytoplasmic or mitochondrial malate dehydrogenase (E.C. 1.1.1.37). I and II showed high Michaelis consts. compared to NAD+ and NADH, but lower (except with III of horse liver) catalytic consts.

L13 ANSWER 158 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 42188-27-2 REGISTRY

CN 3-Pyridinecarboxamide, 1-[5-O-[7-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahapt-1-yl]-.beta.-D-ribofuranosyl]-1,4-dihydro- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

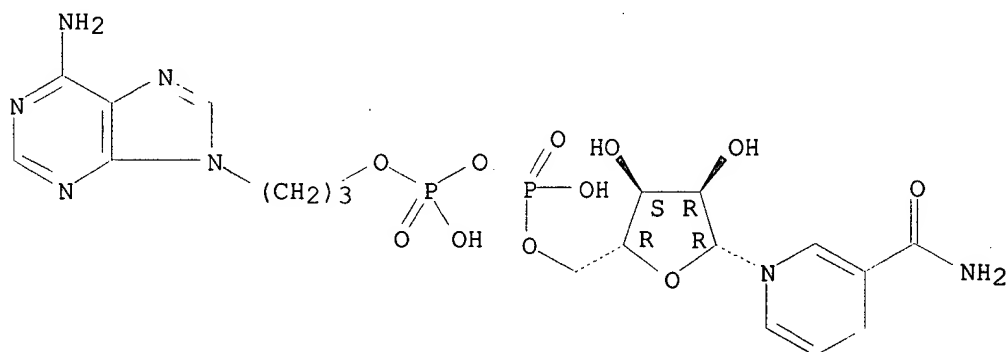
CN Diphosphoric acid, P-[3-(6-amino-9H-purin-9-yl)propyl] ester, P'.fwdarw.5' ester with 1,4-dihydro-1-.beta.-D-ribofuranosyl-3-pyridinecarboxamide

OTHER NAMES:

CN 3-Pyridinecarboxamide, 1-[5-O-[[[[[3-(6-amino-9H-purin-9-yl)propyl]oxy]hydroxyphosphinyl]oxy]hydroxyphosphinyl]-.beta.-D-ribofuranosyl]-1,4-dihydro-

FS STEREOSEARCH
MF C19 H27 N7 O11 P2
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 79:32239 Interactions of the nonfunctional coenzyme binding site in dehydrogenases with [nicotinamide-ribofuranosyl]-[.omega.-(adenin-9-yl)-n-alkyl] pyrophosphates. Jeck, Reinhard; Wilhelm, Gabriele (Chem.-Physiol. Inst., Univ. Frankfurt, Frankfurt/M., Ger.). Justus Liebigs Ann. Chem. (3), 531-43 (German) 1973. CODEN: JLACBF.

GI For diagram(s), see printed CA Issue.

AB The NAD analogs I (n = 2-5) were prepd. by condensation of .omega.-(adenin-9-yl)alkyl pyrophosphate with NMN. I and their enzymically prepd. dihydro derivs. (II) had nearly identical chem. and phys. properties with NAD⁺ and NADH, resp. I and II were active as H acceptors or H donors, resp., with alc. dehydrogenase (E.C. 1.1.1.1) (III) from yeast or horse liver, lactate dehydrogenase (E.C. 1.1.1.27), or cytoplasmic or mitochondrial malate dehydrogenase (E.C. 1.1.1.37). I and II showed high Michaelis consts. compared to NAD⁺ and NADH, but lower (except with III of horse liver) catalytic consts.

L13 ANSWER 159 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 42188-26-1 REGISTRY

CN 3-Pyridinecarboxamide, 1-[5-O-[6-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahex-1-yl]-.beta.-D-ribofuranosyl]-1,4-dihydro- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Diphosphoric acid, P-[2-(6-amino-9H-purin-9-yl)ethyl] ester, P'.fwdarw.5' ester with 1,4-dihydro-1-.beta.-D-ribofuranosyl-3-pyridinecarboxamide

OTHER NAMES:

CN 3-Pyridinecarboxamide, 1-[5-O-[[[[2-(6-amino-9H-purin-9-yl)ethyl]oxy]hydroxyphosphinyl]oxy]hydroxyphosphinyl]-.beta.-D-ribofuranosyl]-1,4-dihydro-

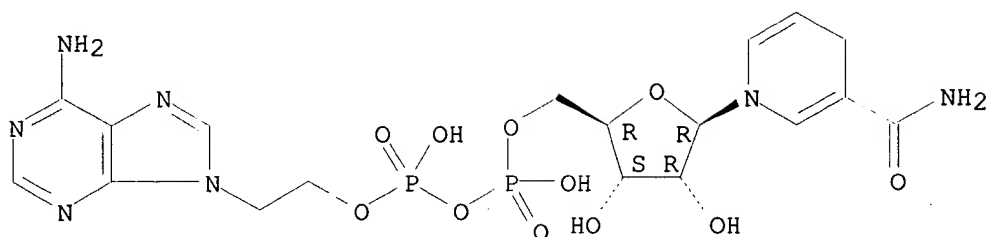
FS STEREOSEARCH

MF C18 H25 N7 O11 P2

LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

Searched by: Mary Hale 308-4258 CM-1 12D16

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 79:32239 Interactions of the nonfunctional coenzyme binding site in dehydrogenases with [nicotinamide-ribofuranosyl]-[.omega.-(adenin-9-yl)-n-alkyl] pyrophosphates. Jeck, Reinhard; Wilhelm, Gabriele (Chem.-Physiol. Inst., Univ. Frankfurt, Frankfurt/M., Ger.). Justus Liebigs Ann. Chem. (3), 531-43 (German) 1973. CODEN: JLACBF.

GI For diagram(s), see printed CA Issue.

AB The NAD analogs I (n = 2-5) were prepd. by condensation of .omega.-(adenin-9-yl)alkyl pyrophosphate with NMN. I and their enzymically prepd. dihydro derivs. (II) had nearly identical chem. and phys. properties with NAD⁺ and NADH, resp. I and II were active as H acceptors or H donors, resp., with alc. dehydrogenase (E.C. 1.1.1.1) (III) from yeast or horse liver, lactate dehydrogenase (E.C. 1.1.1.27), or cytoplasmic or mitochondrial malate dehydrogenase (E.C. 1.1.1.37). I and II showed high Michaelis consts. compared to NAD⁺ and NADH, but lower (except with III of horse liver) catalytic consts.

L13 ANSWER 160 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 42188-25-0 REGISTRY

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[9-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphanon-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[9-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-2,4-dioxo-1,3-diphosphanon-1-yl]-.beta.-D-ribofuranosyl]-, inner salt, P,P'-dioxide

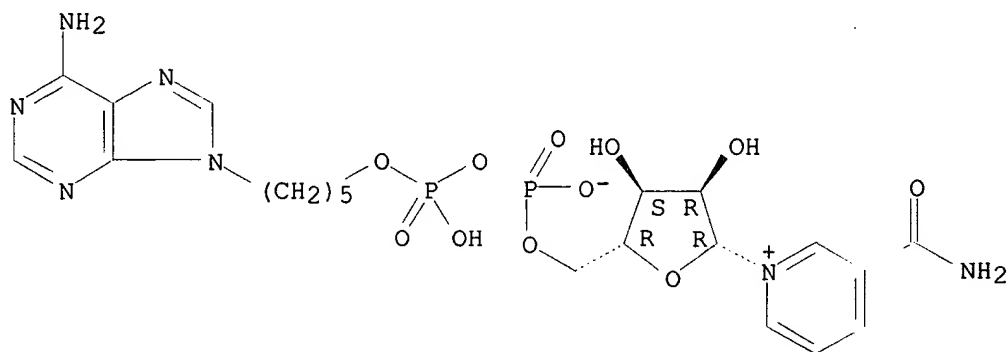
FS STEREOSEARCH

MF C21 H29 N7 O11 P2

LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 105:148757 Kinetics and native and modified liver alcohol dehydrogenase with coenzyme analogs: isomerization of enzyme-nicotinamide adenine dinucleotide complex. Plapp, Bryce V.; Sogin, David C.; Dworschack, Robert T.; Bohlken, David P.; Woenckhaus, Christoph; Jeck, Reinhard (Dep. Biochem., Univ. Iowa, Iowa City, IA, 52242, USA). Biochemistry, 25(19), 5396-402 (English) 1986. CODEN: BICHAW. ISSN: 0006-2960.

AB Coenzyme analogs with the adenosine ribose replaced with n-Pr, n-Bu, and n-pentyl groups, the coenzyme analogs with the adenosine replaced with 3-(4-acetylanilino)propyl and 6-(4-acetylanilino)hexyl moieties, and NMN, nicotinamide hypoxanthine dinucleotide, and 3-acetylpyridine adenine dinucleotide were used in the steady-state kinetic studies with native and activated, amidinated enzymes. The K_m and K_i values increased up to 100-fold upon modification of coenzyme or enzyme. Turnover nos. with NAD and EtOH increased in some cases up to 10-fold due to increased rates of dissocn. of enzyme-reduced coenzyme complexes. Rates of dissocn. of oxidized coenzyme appeared to be most unaffected, but the values calcd. (10-60 s⁻¹) were significantly less than the turnover nos. with Ach and reduced coenzyme (20-900 s⁻¹, at pH 8, 25.degree.). Rates of assocn. of coenzyme analogs also decreased up to 100-fold. When lysine-228 in the adenosine-binding site was picolinimidylated, turnover nos. increased .apprx.10-fold with NAD(H). Furthermore, the pH dependencies for assocn. and dissocn. of NAD and turnover no. with NAD and EtOH showed the fastest rates above a pK value of 8.0. Turnover with NADH and Ach was fastest below a pK value of 8.1. These results could be explained by a mechanism in which isomerization of the enzyme-NAD complex (110 s⁻¹) is partially rate-limiting in turnover with NAD and EtOH (60 s⁻¹) and is controlled by ionization of the H-bonded system that includes the water ligated to the catalytic Zn and the imidazole group of histidine-51.

REFERENCE 2: 79:32239 Interactions of the nonfunctional coenzyme binding site in dehydrogenases with [nicotinamide-ribofuranosyl]-[.omega.-(adenin-9-yl)-n-alkyl] pyrophosphates. Jeck, Reinhard; Wilhelm, Gabriele (Chem.-Physiol. Inst., Univ. Frankfurt, Frankfurt/M., Ger.). Justus Liebigs Ann. Chem. (3), 531-43 (German) 1973. CODEN: JLACBF.

GI For diagram(s), see printed CA Issue.

AB The NAD analogs I (n = 2-5) were prep'd. by condensation of .omega.-(adenin-9-yl)alkyl pyrophosphate with NMN. I and their enzymically prep'd. dihydro derivs. (II) had nearly identical chem. and phys. properties with NAD⁺ and NADH, resp. I and II were active as H acceptors or H donors, resp., with alc. dehydrogenase (E.C. 1.1.1.1) (III) from yeast or horse liver, lactate dehydrogenase (E.C. 1.1.1.27), or cytoplasmic or mitochondrial malate dehydrogenase (E.C. 1.1.1.37). I and

II showed high Michaelis consts. compared to NAD⁺ and NADH, but lower (except with III of horse liver) catalytic consts.

L13 ANSWER 161 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 42188-24-9 REGISTRY

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[8-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxo-2,4-dioxo-1,3-diphosphaoct-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

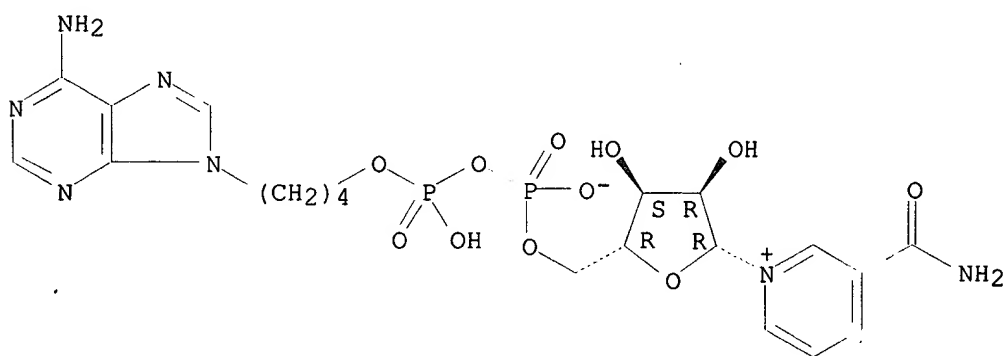
CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[8-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-2,4-dioxo-1,3-diphosphaoct-1-yl]-.beta.-D-ribofuranosyl]-, inner salt, P,P'-dioxide

FS STEREOSEARCH

MF C20 H27 N7 O11 P2

LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.



3 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 109:124886 Changing coenzymes improves oxidations catalyzed by alcohol dehydrogenase. Kazlauskas, Romas J. (Corp. Res. Dev., Gen. Electr. Co., Schenectady, NY, 12301, USA). J. Org. Chem., 53(19), 4633-5 (English) 1988. CODEN: JOCEAH. ISSN: 0022-3263.

GI For diagram(s), see printed CA Issue.

AB The use of coenzyme analogs to optimize enzyme-catalyzed reactions is suggested as a complement to current efforts in enzyme improvement by site-directed mutagenesis. As an example, the oxidn. of EtOH by NAD catalyzed by alc. dehydrogenase from horse liver, E.C. 1.1.1.1, which proceeds poorly due to inhibition by the product acetaldehyde (K_i = 0.6 mM, noncompetitive) was investigated. Substitution of 13 different analogs of NAD identified thionicotinamide adenine dinucleotide (I) and 3-acetylpyridine adenine dinucleotide (II) as useful substitutes for NAD because they show an increased K_i with acetaldehyde (6 mM and 35 mM, resp.). These analogs are com. available, are good substrates for alc. dehydrogenase (V_{max} is 2-fold that with NAD), and can be regenerated using existing procedures (either 2-oxoglutarate/glutamic dehydrogenase or methylene blue and O₂). Small-scale oxidn. of EtOH to acetaldehyde using II as coenzyme yields 9-fold more acetaldehyde than does NAD. Oxidn. of other alcs. (cyclohexanemethanol, benzyl alc., methallyl alc.) with these analogs showed a similar lessening of product inhibition by aldehyde, increase in V_{max}, and higher yields in small-scale synthesis.

REFERENCE 2: 105:148757 Kinetics and native and modified liver alcohol dehydrogenase with coenzyme analogs: isomerization of enzyme-nicotinamide

Searched by: Mary Hale 308-4258 CM-1 12D16

adenine dinucleotide complex. Plapp, Bryce V.; Sogin, David C.; Dworschack, Robert T.; Bohlken, David P.; Woenckhaus, Christoph; Jeck, Reinhard (Dep. Biochem., Univ. Iowa, Iowa City, IA, 52242, USA). Biochemistry, 25(19), 5396-402 (English) 1986. CODEN: BICHAW. ISSN: 0006-2960.

AB Coenzyme analogs with the adenosine ribose replaced with n-Pr, n-Bu, and n-pentyl groups, the coenzyme analogs with the adenosine replaced with 3-(4-acetylanilino)propyl and 6-(4-acetylanilino)hexyl moieties, and NMN, nicotinamide hypoxanthine dinucleotide, and 3-acetylpyridine adenine dinucleotide were used in the steady-state kinetic studies with native and activated, amidinated enzymes. The K_m and K_i values increased up to 100-fold upon modification of coenzyme or enzyme. Turnover nos. with NAD and EtOH increased in some cases up to 10-fold due to increased rates of dissocn. of enzyme-reduced coenzyme complexes. Rates of dissocn. of oxidized coenzyme appeared to be most unaffected, but the values calcd. (10-60 s⁻¹) were significantly less than the turnover nos. with AcH and reduced coenzyme (20-900 s⁻¹, at pH 8, 25.degree.). Rates of assocn. of coenzyme analogs also decreased up to 100-fold. When lysine-228 in the adenosine-binding site was picolinimidylated, turnover nos. increased .apprx.10-fold with NAD(H). Furthermore, the pH dependencies for assocn. and dissocn. of NAD and turnover no. with NAD and EtOH showed the fastest rates above a pK value of 8.0. Turnover with NADH and AcH was fastest below a pK value of 8.1. These results could be explained by a mechanism in which isomerization of the enzyme-NAD complex (110 s⁻¹) is partially rate-limiting in turnover with NAD and EtOH (60 s⁻¹) and is controlled by ionization of the H-bonded system that includes the water ligated to the catalytic Zn and the imidazole group of histidine-51.

REFERENCE 3: 79:32239 Interactions of the nonfunctional coenzyme binding site in dehydrogenases with [nicotinamide-ribofuranosyl]-[.omega.-(adenin-9-yl)-n-alkyl] pyrophosphates. Jeck, Reinhard; Wilhelm, Gabriele (Chem.-Physiol. Inst., Univ. Frankfurt, Frankfurt/M., Ger.). Justus Liebigs Ann. Chem. (3), 531-43 (German) 1973. CODEN: JLACBF.

GI For diagram(s), see printed CA Issue.

AB The NAD analogs I (n = 2-5) were prepd. by condensation of .omega.-(adenin-9-yl)alkyl pyrophosphate with NMN. I and their enzymically prepd. dihydro derivs. (II) had nearly identical chem. and phys. properties with NAD⁺ and NADH, resp. I and II were active as H acceptors or H donors, resp., with alc. dehydrogenase (E.C. 1.1.1.1) (III) from yeast or horse liver, lactate dehydrogenase (E.C. 1.1.1.27), or cytoplasmic or mitochondrial malate dehydrogenase (E.C. 1.1.1.37). I and II showed high Michaelis consts. compared to NAD⁺ and NADH, but lower (except with III of horse liver) catalytic consts.

L13 ANSWER 162 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 42188-23-8 REGISTRY

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[7-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxo-2,4-dioxo-1,3-diphosphahept-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[7-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-2,4-dioxo-1,3-diphosphahept-1-yl]-.beta.-D-ribofuranosyl]-, inner salt, P,P'-dioxide

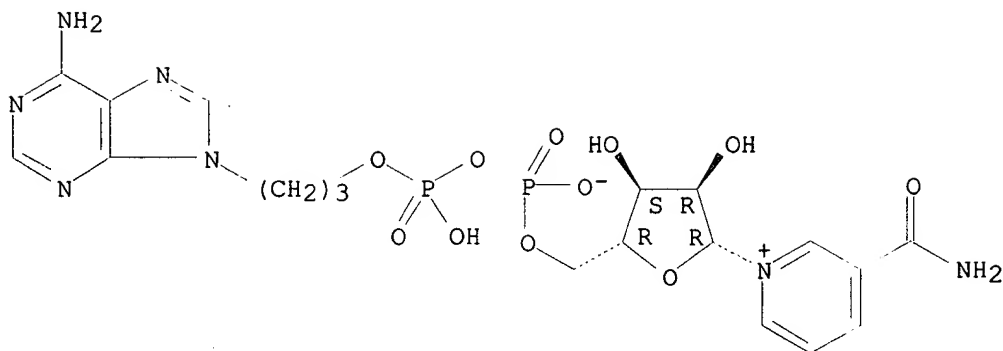
FS STEREOSEARCH

MF C19 H25 N7 O11 P2

LC STN Files: BEILSTEIN*, CA, CAPLUS

(*File contains numerically searchable property data)

Absolute stereochemistry.



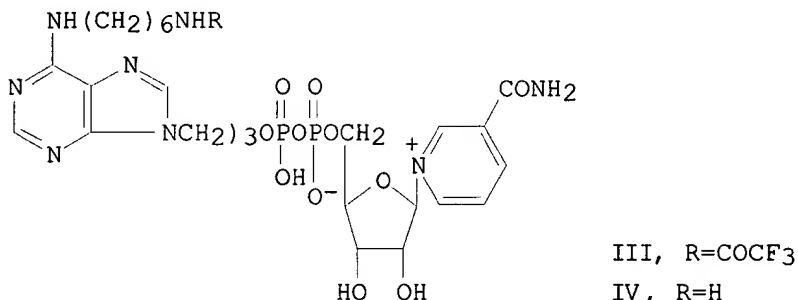
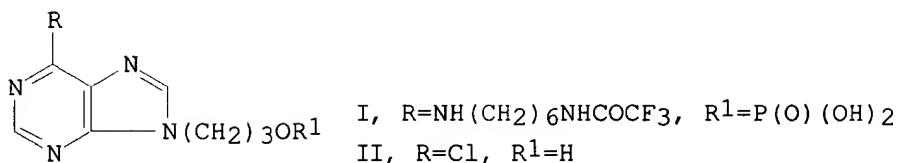
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 105:148757 Kinetics and native and modified liver alcohol dehydrogenase with coenzyme analogs: isomerization of enzyme-nicotinamide adenine dinucleotide complex. Plapp, Bryce V.; Sogin, David C.; Dworschack, Robert T.; Bohlken, David P.; Woenckhaus, Christoph; Jeck, Reinhard (Dep. Biochem., Univ. Iowa, Iowa City, IA, 52242, USA). Biochemistry, 25(19), 5396-402 (English) 1986. CODEN: BICHAW. ISSN: 0006-2960.

AB Coenzyme analogs with the adenosine ribose replaced with n-Pr, n-Bu, and n-pentyl groups, the coenzyme analogs with the adenosine replaced with 3-(4-acetylanilino)propyl and 6-(4-acetylanilino)hexyl moieties, and NMN, nicotinamide hypoxanthine dinucleotide, and 3-acetylpyridine adenine dinucleotide were used in the steady-state kinetic studies with native and activated, amidinated enzymes. The K_m and K_i values increased up to 100-fold upon modification of coenzyme or enzyme. Turnover nos. with NAD and EtOH increased in some cases up to 10-fold due to increased rates of dissocn. of enzyme-reduced coenzyme complexes. Rates of dissocn. of oxidized coenzyme appeared to be most unaffected, but the values calcd. (10-60 s⁻¹) were significantly less than the turnover nos. with AcH and reduced coenzyme (20-900 s⁻¹, at pH 8, 25.degree.). Rates of assocn. of coenzyme analogs also decreased up to 100-fold. When lysine-228 in the adenosine-binding site was picolinimidylated, turnover nos. increased .apprx.10-fold with NAD(H). Furthermore, the pH dependencies for assocn. and dissocn. of NAD and turnover no. with NAD and EtOH showed the fastest rates above a pK value of 8.0. Turnover with NADH and AcH was fastest below a pK value of 8.1. These results could be explained by a mechanism in which isomerization of the enzyme-NAD complex (110 s⁻¹) is partially rate-limiting in turnover with NAD and EtOH (60 s⁻¹) and is controlled by ionization of the H-bonded system that includes the water ligated to the catalytic Zn and the imidazole group of histidine-51.

REFERENCE 2: 88:185183 The coenzyme analog (3-[6-(6-aminohexylamino)-9-purinyl]propyl)(nicotinamide-D-ribose)diphosphate as ligand for affinity chromatography of dehydrogenases. Berariu, Veronica; Jeck, Reinhard; Woenckhaus, Christoph (Gustav-Embden-Zent. Biol. Chem., Univ. Frankfurt, Frankfurt/Main, Ger.). Justus Liebigs Ann. Chem. (1), 118-23 (German) 1978. CODEN: JLACBF. ISSN: 0075-4617.

GI



AB 9-[3-(Dihydroxyphosphoryloxy)propyl]-6-[6-(trifluoroacetyl-amino)hexylamino]-9H-purine (I) was prepd. starting from 6-chloro-9-(3-hydroxypropyl)-9H-purine (II). After condensation of this AMP-analog with dicyclohexylcarbodiimide and NMN in aq. pyridine, a new NAD-analog was formed. The coenzyme analog (3-[6-(6-trifluoroacetylaminohexylamino)-9-purinyl]propyl)(nicotinamide-D-ribose)diphosphate (III) acted as H acceptor (its reduced form as H donor) when tested against different dehydrogenases. Highly dis-socd. complexes between this coenzyme analog and dehydrogenases were formed. Removal of the trifluoroacetyl group led to the unstable coenzyme analog (3-[6-(6-aminohexylamino)-9-purinyl]propyl)(nicotinamide-D-ribose)diphosphate (IV), which can be covalently attached to agarose activated with CNBr. When dehydrogenases were applied to the column of the immobilized AMP and NAD-analogs, only glyceraldehyde 3-phosphate dehydrogenase was retained. Elution of the enzyme occurred only after addn. of KCl to the eluant.

REFERENCE 3: 79:32239 Interactions of the nonfunctional coenzyme binding site in dehydrogenases with [nicotinamide-ribofuranosyl]-[.omega.-(adenin-9-yl)-n-alkyl] pyrophosphates. Jeck, Reinhard; Wilhelm, Gabriele (Chem.-Physiol. Inst., Univ. Frankfurt, Frankfurt/M., Ger.). Justus Liebigs Ann. Chem. (3), 531-43 (German) 1973. CODEN: JLACBF.

GI For diagram(s), see printed CA Issue.

AB The NAD analogs I (n = 2-5) were prepd. by condensation of .omega.-(adenin-9-yl)alkyl pyrophosphate with NMN. I and their enzymically prepd. dihydro derivs. (II) had nearly identical chem. and phys. properties with NAD⁺ and NADH, resp. I and II were active as H acceptors or H donors, resp., with alc. dehydrogenase (E.C. 1.1.1.1) (III) from yeast or horse liver, lactate dehydrogenase (E.C. 1.1.1.27), or cytoplasmic or mitochondrial malate dehydrogenase (E.C. 1.1.1.37). I and II showed high Michaelis consts. compared to NAD⁺ and NADH, but lower (except with III of horse liver) catalytic consts.

L13 ANSWER 163 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 35677-98-6 REGISTRY

CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

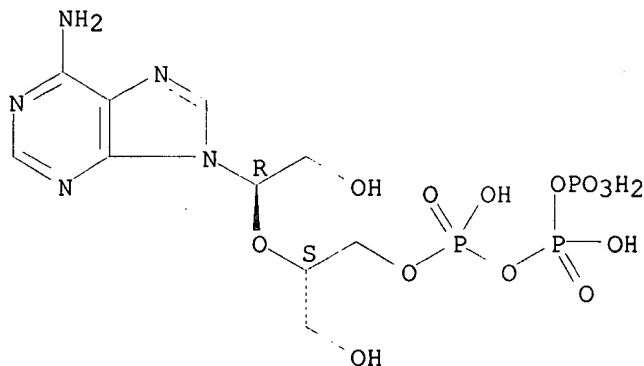
OTHER CA INDEX NAMES:

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, [S-(R*,S*)]-

OTHER NAMES:

CN ATP 2',3'-dialcohol
 CN orATP
 CN rro-ATP
 CN rroATP
 FS STEREOSEARCH
 MF C10 H18 N5 O13 P3
 CI COM
 LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
 (*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1967 TO DATE)
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 13 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 113:70937 Biocompatibility of hemoglobin solutions. II. The inflammatory reaction of human monocytes and mouse peritoneal macrophages. Simoni, Jan; Feola, Mario; Tran, Ruc; Buckner, Mark; Canizaro, Peter C. (Sch. Med., Texas Tech Univ., Lubbock, TX, 79430, USA). Artif. Organs, 14(2), 98-109 (English) 1990. CODEN: ARORD7. ISSN: 0160-564X.
 AB This study explored the inflammatory mechanism of toxicity of Hb solns. (Hb-S). Human monocytes and mouse activated peritoneal macrophages were incubated with seven different solns. The first four consists of non-cross-linked bovine Hb. Of these, Hb-SI was incompletely purified of stromal phospholipids, Hb-SII was contaminated with environmental bacterial endotoxins. Hb-SIII was pure Hb, and Hb-SIV was pure Hb with the addn. of superoxide dismutase (SOD), catalase (CAT), and mannitol (M). The other three solns. were made of pure bovine Hb cross-linked with different agents: Hb-SV, reacted with glutaraldehyde; Hb-SVI reacted with bis-3,5-dibromosalicyl fumarate (DBSF); and Hb-SVII reacted with a ring-opened dialdehyde deriv. of 5'(pyro)-phosphate of adenosine (ATP) (o-ATP). The reaction of monocytes and macrophages was studied in terms of (a) O2-derived radicals, as detd. by the measurement of H2O2 and lipid peroxides; (b) complement factor C3a desArg; (c) 6-keto-prostaglandin F1.alpha. (stable metabolite of prostacyclin); and (d) TxB2 (stable metabolite of thromboxane) released into the culture supernatants. The most significant reactions were obtained with the solns. contaminated with stromal phospholipids or bacterial endotoxins. Pure Hb was less reactive. Further redn. in proinflammatory activity was achieved by the addn. of oxygen radical-scavengers (SOD, CAT, and M), or by the crosslinking of Hb with DBSF or o-ATP.

Searched by: Mary Hale 308-4258 CM-1 12D16

REFERENCE 2: 107:232145 Mapping of the adenosine 5'-triphosphate binding site of type II calmodulin-dependent protein kinase. Kwiatkowski, Ann P.; King, Marita M. (Dep. Chem., Ohio State Univ., Columbus, OH, 43210, USA). Biochemistry, 26(24), 7636-40 (English) 1987. CODEN: BICHAW. ISSN: 0006-2960.

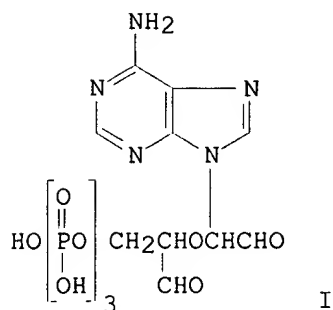
AB The specificity of the ATP-binding site of rat brain type II calmodulin-dependent protein kinase was probed with 25 analogs of ATP modified at various positions in the mol. The analogs were compared by their ability to compete with ATP in the protein kinase reaction. The result of this comparison indicated that the enzyme was most sensitive to modifications at, or replacement of, the purine moiety. Changes at the triphosphate chain were much better tolerated, although, the enzyme exhibited a selective sensitivity to changes in the conformation in this group. The smallest contribution to the specificity of ATP binding appeared to be made by the ribose ring. The K_i values obtained for a subset of these analogs were compared to those previously reported for phosphorylase b kinase and the cyclic nucleotide-dependent protein kinases. A striking similarity in the responses of these protein kinases to modifications of the ATP mol. suggested that the type II calmodulin-dependent protein kinase is related to these enzymes. Support for this conclusion was provided, recently, through comparisons of the deduced primary structures of the .alpha. and .beta. subunits of the type II calmodulin-dependent protein kinase with the protein sequences of the catalytic subunits of phosphorylase b kinase and cAMP-dependent protein kinase which indicated areas of extensive homol.

REFERENCE 3: 103:33140 Derangement of hepatic energy metabolism in lead-sensitized endotoxycosis. Taki, Y.; Shimahara, Y.; Isselhard, W. (Fac. Med., Kyoto Univ., Kyoto, Japan). Eur. Surg. Res., 17(3), 140-9 (English) 1985. CODEN: EUSRBM. ISSN: 0014-312X.

AB Pb-sensitized endotoxycosis was investigated in rats in terms of hepatic energy metab. Pb(OAc)₂ (Pb, 20 mg/kg) or endotoxin (Etx, 4 mg/kg) caused no deaths within 48 h. Pb + Etx resulted in a lethality of 50% and 100% within 6 and 12 h, resp. Etx or Pb alone caused a slight but significant decrease in the hepatic tissue levels of total adenine nucleotides and(or) ATP [35677-98-6] at 3 and 6 h after the application. The energy charge potential (ECP) remained normal. The ketone bodies acetoacetate (AA) [541-50-4] .beta.-hydroxybutyrate (HB) [300-85-6] and their ratio as well as the mitochondrial oxidative phosphorylation tended to increase; the hepatic tissue levels of pyruvate [127-17-3] and lactate [50-21-5] were increased after 3 h, indicative of an accelerated glycolysis. These alterations were no longer detectable after 6 h. In Pb-sensitized endotoxemia (Pb + Etx), the total adenine nucleotides and ATP of the liver tissue decreased to 84% (86%) and 71% (52%) of the controls within 3 and 6 h resp., and the ECP had decreased from 0.865 to 0.684 at 6 h. The ketone bodies were increased, whereas the ratio AA/HB was significantly decreased at 6 h. The hepatic tissue lactate remained elevated. The mitochondrial activity was significantly reduced. A hyperglycemia (175 mg/dL) at 3 h changed into a hypoglycemia (50 mg/dL) at 6 h. Thus, Pb + Etx causes a rapid impairment of hepatic mitochondria which leads to a drastic disturbance of the hepatic energy metab. including hypoglycemia and contributes to an enhanced lethality in Pb-sensitized endotoxycosis.

REFERENCE 4: 99:76807 Modification of hemoglobin-ring opened dials. Greenburg, A. G.; Maffuid, Paul W. (Veterans Adm. Med. Cent., Univ. California, San Diego, CA, 92161, USA). Prog. Clin. Biol. Res., 122(Adv. Blood Substitute Research), 9-17 (English) 1983. CODEN: PCBRD2. ISSN: 0361-7742.

GI



AB The dialdehyde of ATP (I) [35677-98-6] was prepd. by periodate oxidn. of ATP [56-65-5] and reacted with stroma-free Hb (SFH) followed by NaBH₄ redn. The soln. was then oxygenated. The P50 of SFH was 5.0 ton compared to I-SFH of 11.0 ton. In the 50% exchange models in rats, unmodified SFH has a half life of 106 min while SFH-I had a half life of 202 min. In dogs acutely exchanged 50% with I-SFH (90% modified) a plasm Hb half-life of >14 h was obsd. compared to 100 min for unmodified SFH and 140 min for pyridoxal 5-phosphate modified SFH. Unmodified SFH was excreted while I-SFH was retained.

REFERENCE 5: 97:105696 Nucleotide analogs with modified sugar residues in RNA synthesis by RNA polymerase from Escherichia coli. Aivazashvili, V. A.; Bibilashvili, R. Sh.; Florent'ev, V. L. (Inst. Mol. Biol., Moscow, USSR). Mol. Biol. (Moscow), 16(3), 493-8 (Russian) 1982. CODEN: MOBIBO. ISSN: 0026-8984.

AB Triphosphoalkyladenines ppp(CH₂)_nA (I; n = 2-4) and the ATP deriv. (II) inhibited RNA elongation competitively with respect to all 4 natural nucleoside triphosphates, whereas 3'-O-methyl-ATP (III) was a competitive inhibitor only with respect to ATP. I and II were not incorporated into RNA; III was, terminating elongation. The mol. wt. distribution of nascent RNA transcripts of a phage T7 template in the presence of I or II was the same as the normal distribution due to pauses in elongation. This suggests that I and II act by prolonging the natural pauses in RNA formation. This suggestion is supported by the fact that I (n = 3) reduces the rate of chain termination by 3'-O-methyl-GTP. The kinetics of inhibition by I resembled inhibition by inorg. pyrophosphate, which suggests that they interact weakly and reversibly with the substrate-binding site of RNA polymerase.

REFERENCE 6: 97:24150 Preparation, structure, and properties of periodate-oxidized ATP, a potential affinity-labeling reagent. Lowe, Peter N.; Beechey, R. Brian (Dep. Biochem., Chelsea Coll., London, SW3 6LX, UK). Bioorg. Chem., 11(1), 55-71 (English) 1982. CODEN: BOCMBM. ISSN: 0045-2068.

AB Periodate oxidn. of ATP yields a single product which was purified and characterized. Periodate-oxidized ATP (o-ATP) behaves as a single compd. during TLC anal., but NMR spectral studies show that it exists in aq. soln. as an equil. mixt. of 3 dialdehyde monohydrates and a dihydrate. Little free aldehyde is present. The dialdehyde monohydrates are in the form of diastereomeric cyclic hemiacetals. The dialdehyde grouping of o-ATP was reduced with NaBH₄, producing a diol. O-ATP is frequently used in attempts to affinity label nucleotide-binding sites on proteins. The proposed structure of o-ATP is discussed in relation to this use for o-ATP.

REFERENCE 7: 90:35503 Activity of polynucleotide phosphorylase with nucleoside diphosphates containing sugar ring modifications. Hawley, D. M.; Sninsky, J. J.; Bennett, G. N.; Gilham, P. T. (Dep. Biol. Sci., Purdue

Univ., West Lafayette, Indiana, USA). Biochemistry, 17(11), 2082-6 (English) 1978. CODEN: BICHAW. ISSN: 0006-2960.

- AB A no. of nucleoside 5'-diphosphates contg. modifications in their sugar rings were synthesized, and the capacity of these nucleotides to act as substrates for polynucleotide phosphorylase was examd. The 5'-diphosphates of 9- β -D-arabinofuranosyladenine (ara-A) and 3'-deoxyadenosine were prepd. by phosphorylation of the nucleosides with POCl₃ followed by condensation of the resulting 5'-phosphates with inorg. phosphate using 1,1'-carbonyldiimidazole as the activating agent. The 5'-diphosphate of each ox-red nucleoside (a nucleoside in the the C2'-C3' bond has been cleaved) was synthesized by oxidn. of the 2',3'-cis-diol groups in the 5'-diphosphates of adenosine, cytidine, guanosine, and uridine with NaIO₄ followed by the redn. of the resulting dialdehydes with NaBH₄. Similar conditions were also used to prep. the ox-red nucleosides as well as their 5'-phosphates and 5'-triphosphates. In a study of the capacity of modified nucleotides to add to a small oligoribonucleotide in the presence of polynucleotide phosphorylase, 2 classes of activity were exhibited: (1) the addn. of a few residues of the nucleotide as in the case of the diphosphates of ara-A, 2'-deoxynucleosides, and (under certain conditions) 2'-O-(α -methoxyethyl)nucleosides; (2) the addn. of only 1 nucleotide residue as in the case of the diphosphates of the ox-red nucleosides and 3'-deoxyadenosine. The activity displayed by the latter class may be of value as a method for the radioactive labeling of the 3'-terminal ends of polyribonucleotides and RNA.

REFERENCE 8: 89:160853 Interaction of human blood platelets with the 2',3'-dialdehyde and 2',3'-dialcohol derivatives of adenosine 5'-diphosphate and adenosine 5'-triphosphate. Pearce, P. Helen; Wright, Judith M.; Egan, Christopher M.; Scrutton, Michael C. (Dep. Biochem., Univ. London King's Coll., London, Engl.). Eur. J. Biochem., 88(2), 543-54 (English) 1978. CODEN: EJBCAI. ISSN: 0014-2956.

- AB The 2',3'-dialdehyde deriv. of ADP (oADP) at concns. approaching the millimolar range induces human blood platelets to undergo shape change, but is incapable of inducing aggregation. When incubated with platelets for 1 min before addn. of the agonist, oADP acts as a competitive inhibitor of shape change and aggregation induced by ADP. Under these conditions secretion and hence aggregation induced by low concns. of collagen, and secretion and hence secondary aggregation induced by adrenaline, thrombin and vasopressin are also inhibited by this analog. In addn., oADP stimulates the rate of primary aggregation induced by adrenaline and causes partial inhibition of primary aggregation induced by thrombin or vasopressin. When longer preincubation times are employed the extent of inhibition with respect to all agonists, except for high concns. of collagen, is increased and the competitive character of the inhibition with respect to ADP is no longer apparent. Incubation of human platelets with the 2',3'-dialdehyde deriv. of ATP (oATP) causes effects similar to those for oADP except that the analog neither induces platelet shape change, nor stimulates the rate of primary aggregation induced by adrenaline. In addn. oATP fails to cause significant inhibition of platelet shape change induced by serotonin. The inhibition caused by oATP is not a function of the time of incubation. The 2',3'-dialc. derivs. of ADP and ATP (orADP and orATP) effect the aggregation properties of human blood platelets in a manner generally resembling those obsd. for the 2',3'-dialdehyde analogs. However, orADP is only weakly effective in causing platelet shape change and stimulating the rate of primary aggregation induced by adrenaline and does not inhibit secretion induced by adrenaline, collagen, thrombin, and vasopressin. The inhibition by orADP increases only slightly with increased time of incubation. Apparently, oADP acts as a partial agonist, whereas oATP and orADP as antagonists for the platelet ADP receptor.

REFERENCE 9: 89:38633 Substrate specificity of soluble mitochondrial ATPase.

Kozlov, I. A.; Metel'skaya, V. A.; Mikhailov, S. N.; Novikova, I. Yu.; Florent'ev, V. L. (Dep. Bioenerg., A. N. Belozerskii Lab. Bioorg. Chem. Mol. Biol., Moscow, USSR). Biokhimiya (Moscow), 43(4), 702-7 (Russian) 1978. CODEN: BIOHAO. ISSN: 0006-307X.

AB The parameters of the hydrolysis of ATP and several analogs by sol. mitochondrial ATPase (I) were detd. The Vmax of the reaction decreased as follows: 2'-deoxy-ATP > ATP > etheno-ATP > GTP > 3'-O-methyl-ATP > UTP. ATP, 2'-deoxy-ATP, 3'-O-methyl-ATP, GTP, and etheno-ATP were hydrolyzed by I with similar apparent Km values. CTP was not hydrolyzed by I and did not inhibit the I reaction at a concn. of 10-2M. Nucleoside triphosphate derivs. with an open ribose ring, 9-[1',5'-dihydroxy-4'-(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]adenine-5'-triphosphate and 1-[1',5'-dihydroxy-4'-(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]cytosine-5'-triphosphate, were effective inhibitors of ATPase (Ki .apprx.5 .times. 10-5 M). I bound ATP analogs having hydrocarbon radicals, (CH2)2, (CH2)3, and (CH2)4, instead of the ribose residues. 9-(3'-Hydroxypropyl)-adenine-3'-triphosphate and 9-(4-hydroxybutyl)adenine-4'-triphosphate were not hydrolyzed by I, although they inhibited the I reaction (Ki = 2 .times. 10-4 M). 9-(2'-Hydroxyethyl)adenine-2'-triphosphate was hydrolyzed by I 8-fold more slowly than ATP. It is suggested that the hydrolysis of substrates of I is preceded by the binding of the substrates in a strained conformation in the active site.

REFERENCE 10: 88:46897 Enzymic incorporation of ATP and CTP analogs into the 3' end of tRNA. Sprinzl, Mathias; Sternbach, Hans; Von der Haar, Friedrich; Cramer, Friedrich (Abt. Chem., Max-Planck-Inst. Exp. Med., Goettingen, Ger.). Eur. J. Biochem., 81(3), 579-89 (English) 1977. CODEN: EJBCAI.

AB Structural analogs of ATP and CTP were investigated as substrates for ATP(CTP):tRNA nucleotidyltransferase (I). Eight out of 26 ATP analogs and 6 out of 9 CTP analogs were incorporated into the 3' terminus of tRNA. In general, for the recognition of the substrates the modification of the cytidine is less crit. than is the modification of adenosine. An isosteric substitution on the ribose residue is possible in both CTP and ATP. The free hydroxyls of these triphosphates can be replaced by an NH2 group or H without loss of substrate properties. Modifications of positions 1, 2, 6, and 8 on the adenine ring of ATP are not allowed whereas modification on positions 2, 4, and 5 on the cytosine ring of CTP are tolerated by I. No differences can be obsd. in the substrate properties of I of different sources. Methods of prepn. of tRNA species, which are shortened at their 3' end by .gtoreq.1 nucleotide, and anal. procedures for characterization of these modified tRNAs are described.

L13 ANSWER 164 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 21134-36-1 REGISTRY

CN Pyridinium, 3-carbamoyl-1-[formyl(1-formyl-2-hydroxyethoxy)methyl]-, trihydrogen pyrophosphate (ester), hydroxide, inner salt, monoester with 6-amino-.alpha.-(1-formyl-2-hydroxyethoxy)-9H-purine-9-acetaldehyde (8CI) (CA INDEX NAME)

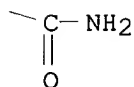
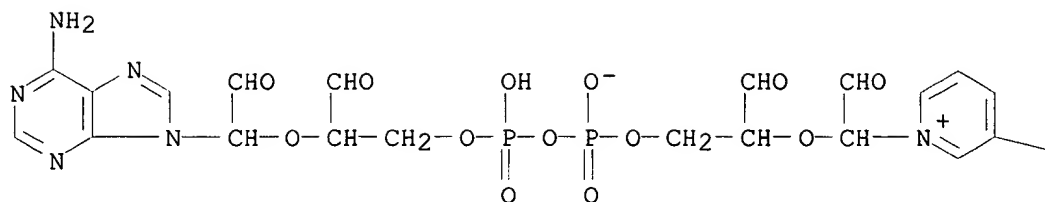
OTHER CA INDEX NAMES:

CN 9H-Purine-9-acetaldehyde, 6-amino-.alpha.-(1-formyl-2-hydroxyethoxy)-, monoester with 3-carbamoyl-1-[formyl(1-formyl-2-hydroxyethoxy)methyl]pyridinium trihydrogen pyrophosphate (ester), hydroxide, inner salt

FS 3D CONCORD

MF C21 H23 N7 O14 P2

LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 69:97105 .alpha.-L-(9-AdeninyI)-.alpha.'-D-(hydroxymethyl)
diglycolaldehyde phosphate esters. Alburn, Harvey E.; Dvorch, William
(American Home Products Corp.). U.S. US 3395148 19680730, 3 pp.
Continuation-in-part of U.S. 3317535 (English). CODEN: USXXAM.
APPLICATION: US 19670306.

GI For diagram(s), see printed CA Issue.

AB Diglycolic aldehyde phosphates (I), with antiinflammatory activity, are
prepd. by the periodic acid oxidn. of adenosine mono-, di- and
triphosphates, and diphosphopyridine nucleotide. Thus, 14.2 g.
5'-adenylic acid was oxidized with 450 ml. 0.1M periodic acid 1 hr. at
25.degree. in the dark. Then, 69 ml. of the soln. was passed over a
Dowex-1-acetate column and the column washed with 3 vols. of H2O. The
self-eluate and wash were freeze-dried to yield 8.5 g. I (R = H, n = 1).
Similarly prepd. were I (R, n given) H, 2; H, 3; A, 2.

L13 ANSWER 165 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 21134-35-0 REGISTRY

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

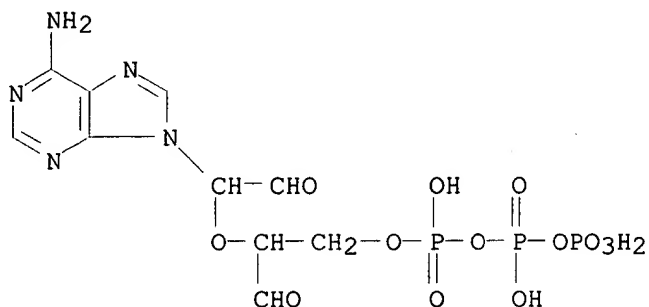
OTHER CA INDEX NAMES:

CN 9H-Purine-9-acetaldehyde, 6-amino-.alpha.-(1-formyl-2-hydroxyethoxy)-, tetrahydrogen triphosphate (ester) (8CI)

FS 3D CONCORD

MF C10 H14 N5 O13 P3

LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:245687 Immunotherapy screening, prognosis, and treatment methods and compositions. Eisenthal, Avi; Shinitzky, Meir; Gonenne, Amnon (Immunotherapy, Inc., USA; Yeda Research and Development Corporation, Ltd.). PCT Int. Appl. WO 9625664 A1 19960822, 121 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US1876 19960212. PRIORITY: US 1995-392553 19950217; US 1995-481857 19950607.

AB The invention describes an immunogen or immunogenic prep. derived from cells, cell membranes or proteins therefrom, that have been modified by treatment with a 2',3'-nucleoside or nucleotide dialdehyde crosslinking agent and by exposure to hydrostatic pressure. The pressure and crosslinker treatment of cells performed in accordance with the invention is termed "PCL-modification". Improved immunogenicity is obtained if the cells are treated with pressure at the same time that they are subjected to the protein crosslinking compds. The cells suitable for PCL-modification in accordance with the invention and for use as immunogens may be tumor or cancer cells, transformed cells, virus-infected or microorganism-infected cells, e.g., bacteria, parasites, yeast, and the like. The PCL-modified tumor or infected cells are esp. capable of inducing and eliciting a specific and potent immune response against the resp. tumor cells, infected cells, or other wise altered cells in both animals and human patients. Human peripheral blood mononuclear cells (PBMC) are sensitized and specifically stimulated to immunoreact against PCL-modified tumor or infected cells as detd. by in vitro sensitization assays. Such assays, alone and in combination with PBMC cytokine analyses, serve as prognostic means to det. or identify those patients who will either respond or will not respond to PCL-immunotherapies and treatments, both in vitro and in vivo. In example, 2',3'-adenosine dialdehyde-modified and hydrostatic pressure-treated leukemia T cell EL4 and other tumor cells were prepd. as vaccine for enhancing cellular immune responses.

REFERENCE 2: 69:97105 .alpha.-L-(9-AdeninyI)-.alpha.'-D-(hydroxymethyl) diglycolaldehyde phosphate esters. Alburn, Harvey E.; Dvornich, William (American Home Products Corp.). U.S. US 3395148 19680730, 3 pp. Continuation-in-part of U.S. 3317535 (English). CODEN: USXXAM. APPLICATION: US 19670306.

GI For diagram(s), see printed CA Issue.

AB Diglycolic aldehyde phosphates (I), with antiinflammatory activity, are prepd. by the periodic acid oxidn. of adenosine mono-, di- and triphosphates, and diphosphopyridine nucleotide. Thus, 14.2 g. 5'-adenylic acid was oxidized with 450 ml. 0.1M periodic acid 1 hr. at 25.degree. in the dark. Then, 69 ml. of the soln. was passed over a Dowex-1-acetate column and the column washed with 3 vols. of H₂O. The self-eluate and wash were freeze-dried to yield 8.5 g. I (R = H, n = 1). Similarly prepd. were I (R, n given) H, 2; H, 3; A, 2.

L13 ANSWER 166 OF 166 REGISTRY COPYRIGHT 2002 ACS

RN 21134-34-9 REGISTRY

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

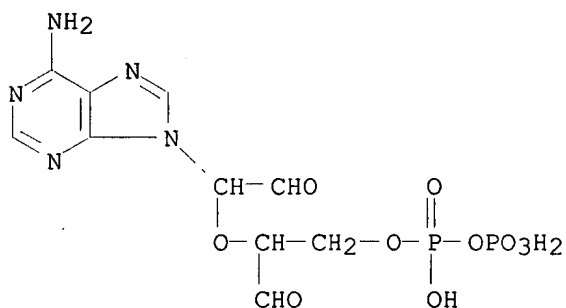
OTHER CA INDEX NAMES:

CN 9H-Purine-9-acetaldehyde, 6-amino-.alpha.-(1-formyl-2-hydroxyethoxy)-, trihydrogen pyrophosphate (ester) (8CI)

FS 3D CONCORD

MF C10 H13 N5 O10 P2

LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIADB, TOXCENTER
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:245687 Immunotherapy screening, prognosis, and treatment methods and compositions. Eisenthal, Avi; Shinitzky, Meir; Gonenne, Amnon (Immunotherapy, Inc., USA; Yeda Research and Development Corporation, Ltd.). PCT Int. Appl. WO 9625664 A1 19960822, 121 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US1876 19960212. PRIORITY: US 1995-392553 19950217; US 1995-481857 19950607.

AB The invention describes an immunogen or immunogenic prepn. derived from cells, cell membranes or proteins therefrom, that have been modified by treatment with a 2',3'-nucleoside or nucleotide dialdehyde crosslinking agent and by exposure to hydrostatic pressure. The pressure and crosslinker treatment of cells performed in accordance with the invention is termed "PCL-modification". Improved immunogenicity is obtained if the cells are treated with pressure at the same time that they are subjected to the protein crosslinking compds. The cells suitable for PCL-modification in accordance with the invention and for use as immunogens may be tumor or cancer cells, transformed cells, virus-infected

or microorganism-infected cells, e.g., bacteria, parasites, yeast, and the like. The PCL-modified tumor or infected cells are esp. capable of inducing and eliciting a specific and potent immune response against the resp. tumor cells, infected cells, or other wise altered cells in both animals and human patients. Human peripheral blood mononuclear cells (PBMC) are sensitized and specifically stimulated to immunoreact against PCL-modified tumor or infected cells as detd. by in vitro sensitization assays. Such assays, alone and in combination with PBMC cytokine analyses, serve as prognostic means to det. or identify those patients who will either respond or will not respond to PCL-immunotherapies and treatments, both in vitro and in vivo. In example, 2',3'-adenosine dialdehyde-modified and hydrostatic pressure-treated leukemia T cell EL4 and other tumor cells were prepd. as vaccine for enhancing cellular immune responses.

REFERENCE 2: 102:22733 Continuous ATP regeneration process with stable acetate kinase. Nakajima, Hiroshi; Nagata, Kazuhiko; Kondo, Hitoshi; Imahori, Kazutomo (Res. Dev. Cent., Unitika Ltd., Uji, 611, Japan). J. Appl. Biochem., 6(1-2), 19-28 (English) 1984. CODEN: JABIDV. ISSN: 0161-7354.

AB Heat-stable acetate kinase (AK) [9027-42-3] from *Bacillus stearothermophilus* was successfully immobilized covalently to Sepharose resin by several conventional methods including carbodiimide, hydroxysuccinimide, CNBr, and glutaraldehyde and also by a new method which utilizes a bifunctional ADP deriv. [21134-34-9] as a spacer. The latter method gave a higher yield in terms of enzyme activity than the conventional methods. The properties and kinetics of the immobilized AK were studied batchwise and in a column. The Michaelis-Menten equation could be applied to the immobilized AK column. The apparent Km values of ADP and acetyl phosphate for immobilized AK were not significantly different from those for free AK. The pH-activity profile of immobilized AK was similar to that of free AK. The heat stability of immobilized AK was markedly improved as compared with free AK. The immobilized AK retained >80% of the initial activity after continuous operation at 30.degree. for 1 mo. The immobilized AK from *B. stearothermophilus* could be utilized as an ATP [56-65-5] regeneration system in the bioreactor.

REFERENCE 3: 69:97105 .alpha.-L-(9-AdeninyI)-.alpha.'-D-(hydroxymethyl) diglycolaldehyde phosphate esters. Alburn, Harvey E.; Dvonch, William (American Home Products Corp.). U.S. US 3395148 19680730, 3 pp. Continuation-in-part of U.S. 3317535 (English). CODEN: USXXAM. APPLICATION: US 19670306.

GI For diagram(s), see printed CA Issue.

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=> fil hcaplus;s 113
COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 796.03 | 796.62 |

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
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L14 233 L13

=> d 167-233 cbib abs hitstr

L14 ANSWER 167 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1983:435108 Document No. 99:35108 The mechanism of inhibition of avian myeloblastosis virus reverse transcriptase by a dialdehyde derivative of ATP. Inactivation of essential sulfhydryl group function. Srivastava, Shiv K.; Abraham, Kakkudiyil I.; Modak, Mukund J. (Meml. Sloan Kettering Cancer Cent., New York, NY, 10021, USA). Biochim. Biophys. Acta, 745(2), 194-201 (English) 1983. CODEN: BBACAQ. ISSN: 0006-3002.

AB The dialdehyde deriv. of ATP inhibits DNA synthesis by avian myeloblastosis virus (AMV) reverse transcriptase (I), whereas the polymerase-assocd. RNase H activity is significantly resistant to this reagent. Neither ATP nor its dialc. form effectively block DNA synthesis, indicating that the aldehyde moiety is required for inhibition. The nature of the reactivity of dialdehyde-ATP with AMV I was examd. Inhibition is noncompetitive with respect to substrate deoxynucleoside triphosphate concn., suggesting that dialdehyde-ATP does not react at the substrate binding site. Pretreatment of I with dialdehyde-ATP or SH group-binding reagents results in the complete loss of its template binding activity; however, treatment of preformed enzyme-template-primer complex with both inhibitors did not dissoc. this complex. The inhibitory effect of dialdehyde-ATP was completely reversed upon addn. of reducing agents, such as dithiothreitol and NaBH₄, indicating that dialdehyde-ATP reacts with the SH groups present in AMV I. Comparative studies carried out with the classical SH reagent, dithiobisnitrobenzoic acid, revealed a remarkable similarity in its action to that of dialdehyde-ATP. Thus, the dialdehyde ATP-mediated inhibition of AMV I is effected via blockage of essential SH groups present in the enzyme protein.

IT 54970-91-1

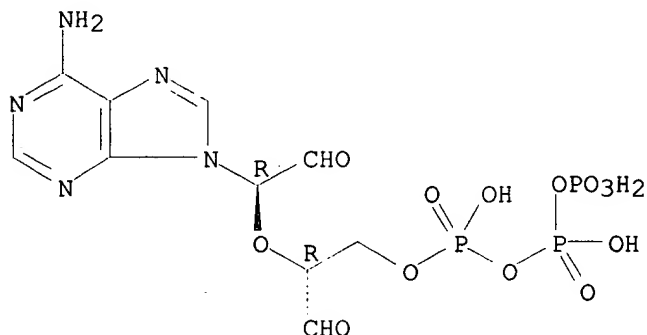
RL: BIOL (Biological study)

(reverse transcriptase of avian myeloblastosis virus inhibition by, sulfhydryl groups in relation to)

Searched by: Mary Hale 308-4258 CM-1 12D16

RN 54970-91-1 HCAPLUS
CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 168 OF 233 HCAPLUS COPYRIGHT 2002 ACS
1983:194112 Document No. 98:194112 Affinity modification of creatine kinase from rabbit skeletal muscle by 2',3'-dialdehyde derivatives of ADP and ATP. Nevinskii, G. A.; Gazaryants, M. G.; Mkrtchyan, Z. S. (Novosibirsk Inst. Org. Chem., Novosibirsk, USSR). Bioorg. Khim., 9(4), 487-95 (Russian) 1983. CODEN: BIKHD7.

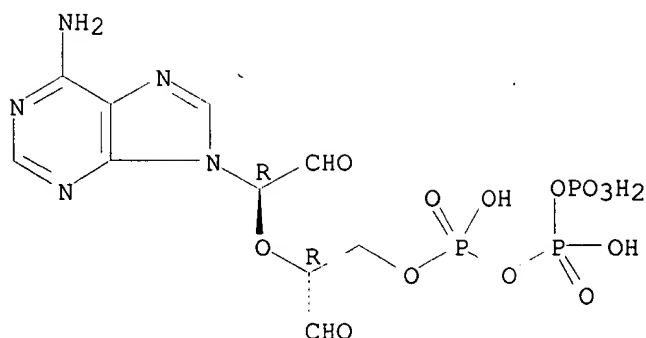
AB Periodate-oxidized ADP and ATP (oADP and oATP) are substrates and affinity reagents for creatine kinase from rabbit skeletal muscle. Both oADP and oATP modified a lysine .epsilon.-amino group in the nucleotide-binding site of the enzyme. Complete inactivation was obsd. upon binding 2 mol oADP/mol of the enzyme dimer. Modification with oADP was described by a linear dependence of the log of enzyme activity on time, indicating a pseudo-1st-order reaction. The reaction rate const. (kt = 8 .times. 103 min-1) and dissocn. const. for the reversible enzyme-oADP complex (Kd = 62 .mu.M) were detd. ADP protected the enzyme from inactivation and covalent binding of the analog, whereas oADP covalently bound to the enzyme was phosphorylated by phosphocreatine. The data obtained suggest that the .epsilon.-amino group of a lysine residue of the active site is located in close proximity to ribose of ATP and ADP forming a complex with the enzyme. This group seems essential for correct orientation of the nucleotide polyphosphate chain in the enzyme active center, but takes no immediate part in the transphosphorylation process.

IT 54970-91-1 64060-84-0

RL: BIOL (Biological study)
(creatine kinase affinity labeling by, lysine in)

RN 54970-91-1 HCAPLUS
CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

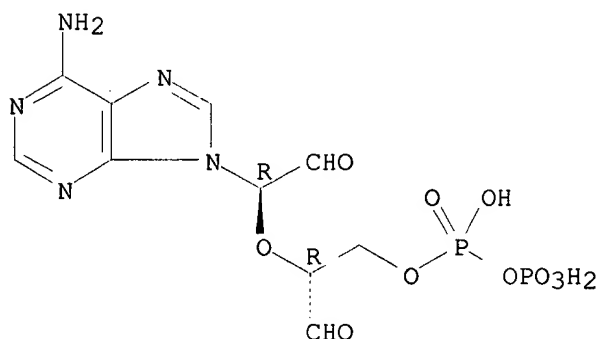
Absolute stereochemistry.



RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 169 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1983:193997 Document No. 98:193997 Regulation by nucleotides and phosphate of mitochondrial ATP hydrolysis and ATP synthesis. Godinot, Catherine; Di Pietro, Attilio; Penin, Francois; Baubichon, Helene; Gautheron, Daniele C. (Lab. Biol. Technol. Membr., Univ. Claude Bernard de Lyon, Villeurbanne, 69622, Fr.). Biochem. Metab. Processes, Proc. Steenbock-Lilly Int. Symp., Meeting Date 1982, 451-64. Editor(s): Lennon, Doris L. F.; Stratman, Frederick W.; Zahlten, Rainer N. Elsevier: New York, N. Y. (English) 1983. CODEN: 49OLAG.

AB The characteristics of the inhibition of pig heart mitochondrial F1 ATPase induced by preincubation of F1 with ADP followed by hydrolysis of MgATP are described by a previously proposed model scheme (Di Pietro, A., et al., 1980), and the effects of ADP and PO43- binding to regulatory sites of F1 in the F1F0 complex are discussed. Satn. of the specific regulatory site of F1 by ADP in the presence of Mg2+ induces a conformational change in the enzyme to a form with low ATPase activity. Addn. of MgATP to ADP-bound F1 results in a further change in enzyme conformation and activity. The limited inhibition of the F1F0 complex under conditions similar to those of F1 alone is attributed to prior satn. of F1 ADP regulatory sites in the complex and indicates that, in the complex, F1 has a conformation rather inactive toward MgATP. In the F1F0 complex, the coupling efficiency between ATP synthesis and nucleotide triphosphate hydrolysis is regulated by ADP and PO43-. In newborn calf liver mitochondria, the coupling efficiency between succinate oxidn. and ATP synthesis is enhanced by ATP and increasing PO43- concn.

IT 64060-84-0

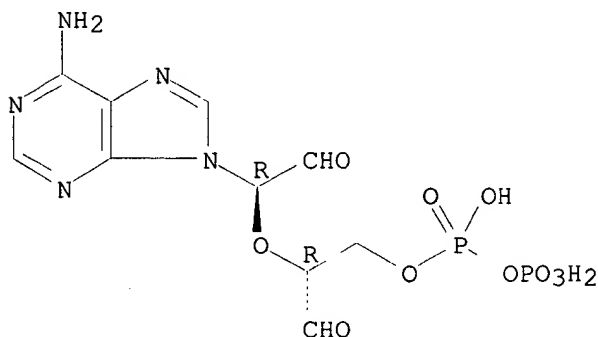
Searched by: Mary Hale 308-4258 CM-1 12D16

RL: BIOL (Biological study)
(ATPase interaction with, adenine nucleotide binding site in relation to)

RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 170 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1983:173408 Document No. 98:173408 Interaction of chick oviduct progesterone receptor with the 2',3'-dialdehyde derivatives of adenosine 5'-triphosphate. McBlain, W. A.; Toft, D. O. (Dep. Cell Biol., Mayo Clin., Rochester, MN, 55905, USA). Biochemistry, 22(9), 2262-70 (English) 1983. CODEN: BICHAW. ISSN: 0006-2960.

AB Avian oviduct progesterone [57-83-0] receptor was treated with the 2',3'-dialdehyde deriv. of ATP (oATP) [54970-91-1] in an attempt to demonstrate the presence of nucleotide binding sites on the receptor. When added to cytosol, oATP inhibiting binding by transformed receptor to ATP-Sepharose, DNA-cellulose, phosphocellulose, or isolated nuclei in an irreversible manner. The oATP did not disrupt the steroid-receptor complex, but it did alter the ionic properties of the receptor. This was demonstrated by an increased affinity of receptor for DEAE-cellulose and for hydroxylapatite. The effect of oATP [56-65-5] on progesterone receptor was mimicked by oATP with regard to 2 properties: it altered the rate of receptor inactivation that occurs in the absence of progesterone, and it promoted receptor conversion from an 8 S complex to lower sedimenting forms (4-6 S). The action of oATP on the receptor could be blocked by the addn. of pyridoxal 5'-phosphate [54-47-7]. A partial interference of oATP action was also obsd. when ATP was added. Thus, oATP interacts with the progesterone receptor and may be used as an affinity-labeling agent for receptor characterization.

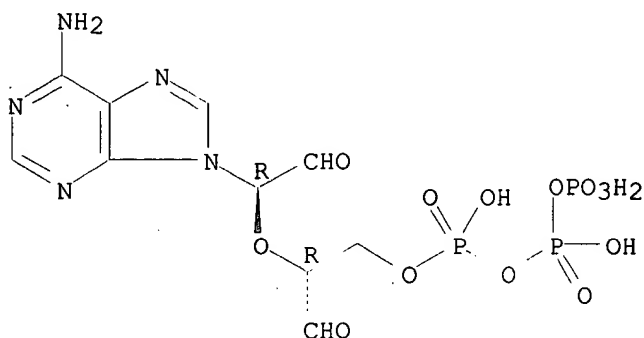
IT 54970-91-1

RL: BIOL (Biological study)
(progesterone receptor properties in response to)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 171 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1983:121988 Document No. 98:121988 Affinity labeling of nicotinamide adenine dinucleotide-dependent isocitrate dehydrogenase by the 2',3'-dialdehyde derivative of adenosine 5'-diphosphate. Evidence for the formation of an unusual reaction product. King, Marita M.; Colman, Roberta F. (Dep. Chem., Univ. Delaware, Newark, DE, 19711, USA). Biochemistry, 22(7), 1656-65 (English) 1983. CODEN: BICHAW. ISSN: 0006-2960.

AB Modification of pig heart NAD-dependent isocitrate dehydrogenase (I) by the 2',3'-dialdehyde deriv. of ADP (II) resulted in a time-dependent inactivation of the enzyme. Two kinetically distinct phases were obsd. for the loss in I activity with max. rate consts. of 0.38 and 0.023 min⁻¹, at satg. concns. of II, at pH 7.0 and in the presence of 2.0 mM MnSO₄. The K_i values for both phases of the reaction were very similar; an av. of 22.9 .mu.M for free II was obtained with consts. detd. in the presence of 0.2, 0.3, and 2.0 mM MnSO₄. At pH 7.0 and in the presence of Mn²⁺, almost complete protection of I from inactivation by II was provided by ADP and isocitrate, whereas only partial protection was afforded by NADH and ATP; NAD was without effect. Only the protection by ADP was consistent with its directly detd. binding const. which may indicate that isocitrate, NADH, and ATP exert allosteric effects on the inactivation by II, whereas ADP may compete with II for the same nucleotide-binding site. Affinity labeling of I with [14C]II resulted in radioactive labeling of the 3 distinct subunits. The incorporation of .apprx.1 mol [14C]II/mol av. subunit corresponded to total inactivation of I. Inactivation of I by II resulted in the formation of a I-II product that was unaffected by subsequent reaction with NaBH₄ which suggests that the reaction product with I was not the generally expected Schiff base. Formation of the relatively stable product involved a loss of the pyrophosphoryl group of II as demonstrated by a comparison of the stoichiometry of the reaction detd. with [14C]II and [32P]II. Further evidence obtained in this study was consistent with the formation of a 4',5'-didehydro-2',3'-dihydroxymorpholino deriv. between II and the .epsilon.-amino group of lysine on I. The results suggest that an allosteric site for ADP is present on each type of I subunit and that the structurally distinct subunits may be functionally similar.

IT 64060-84-0

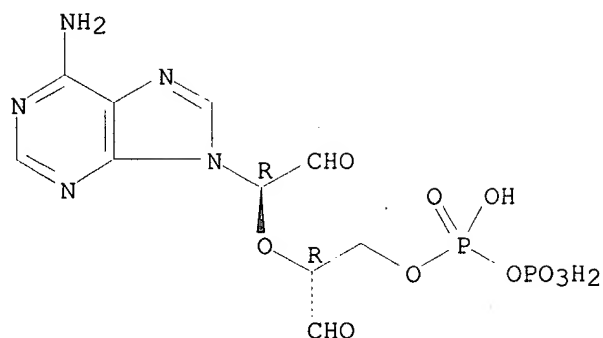
RL: BIOL (Biological study)

(isocitrate dehydrogenase affinity labeling with, subunit interactions in relation to)

RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 172 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1983:89799 Document No. 98:89799 Borohydride reduction of periodate-oxidized nucleotides; isolation and structure of the reduction intermediate. Rosenthal, Luann P.; Hogenkamp, Harry P. C.; Bodley, James W. (Dep. Biochem., Univ. Minnesota, Minneapolis, MN, 55455, USA). Carbohydr. Res., 111(1), 85-91 (English) 1982. CODEN: CRBRAT. ISSN: 0008-6215.

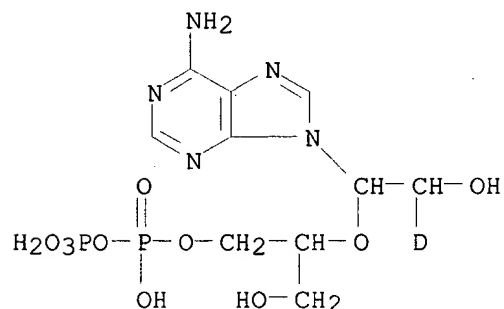
AB The redn. of periodate-oxidized nucleotides with NaBH₄ proceeds via a reaction intermediate presumed to be a monoalc. The borohydride-redn. intermediate of periodate-oxidized ADP has been isolated by anion-exchange, liq. chromatog., and subjected to redn. Redn. by NaBH₄ and NaBD₄ showed that the 2 aldehyde groups are sequentially reduced in the order 3' and 2', and that the isolated intermediate corresponds to the semi-reduced, 3'-alc., 2'-aldehyde deriv. This compd. is a useful analog for the study of enzymes and proteins that interact with nucleotides.

IT 84659-22-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and borohydride and redn. of)

RN 84659-22-3 HCAPLUS

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy-2-d]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)



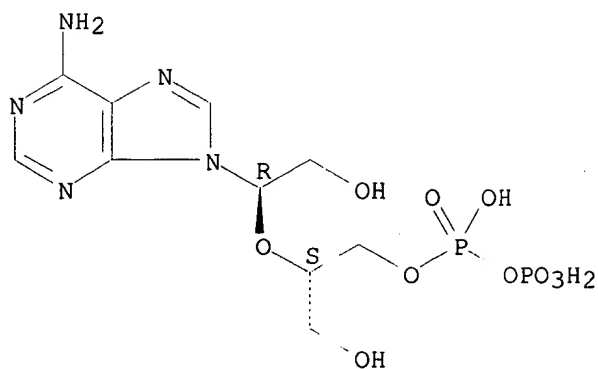
IT 58176-57-1P 64060-84-0P 84659-21-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and borohydride redn. of)

RN 58176-57-1 HCAPLUS

CN Diphosphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

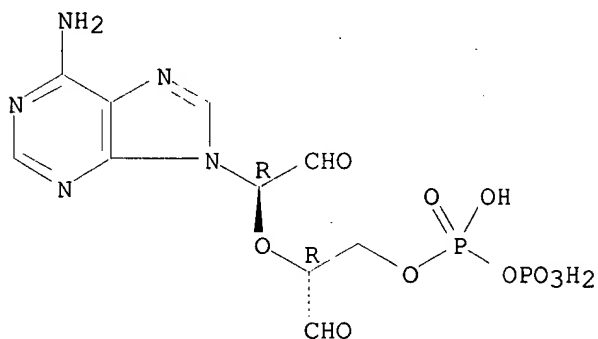
Absolute stereochemistry.



RN 64060-84-0 HCAPLUS

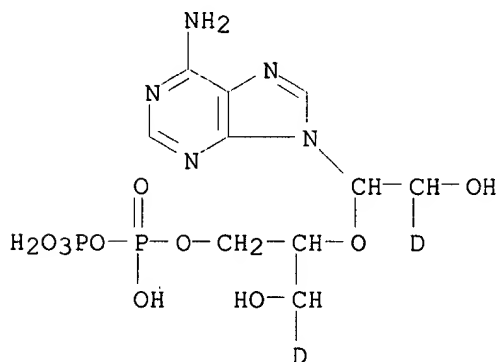
CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 84659-21-2 HCAPLUS

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy-2-d]-3-hydroxypropyl-3-d] ester (9CI) (CA INDEX NAME)



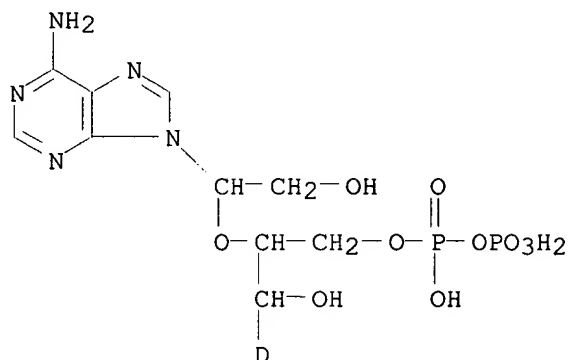
IT 84659-23-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 84659-23-4 HCAPLUS

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl-3-d] ester (9CI) (CA INDEX NAME)

Searched by: Mary Hale 308-4258 CM-1 12D16



L14 ANSWER 173 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1983:49500 Document No. 98:49500 Phenol sulfotransferase. II. Inactivation by phenylglyoxal, N-ethylmaleimide and ribonucleotide 2',3'-dialdehydes. Borchardt, Ronald T.; Schasteen, Charles S.; Wu, Su Er (Smissman Res. Lab., Univ. Kansas, Lawrence, KS, 66045, USA). Biochim. Biophys. Acta, 708(3), 280-93 (English) 1982. CODEN: BBACAQ. ISSN: 0006-3002.

AB Phenylglyoxal rapidly inactivated rat liver phenol sulfotransferase (EC 2.8.2.1) (I). Enzyme inactivation was accompanied by incorporation of 1.5 mol [7-¹⁴C]phenylglyoxal/mol enzyme. 3'-Phosphoadenosine 5'-phosphosulfate (PAPS), the sulfate donor, prevented inactivation and decreased [7-¹⁴C]phenylglyoxal incorporation to 0.78 mol/mol enzyme. N-Ethylmaleimide also caused rapid inactivation of I with concomitant incorporation of 2.35 mol N-[³H]ethylmaleimide/mol enzyme. Thus, arginine residues may be anionic recognition sites for PAPS, and essential SH residues are present on phenol sulfotransferase. Ribonucleotide dialdehydes, but not the corresponding 2',3'-acyclic nucleotides, produced rapid and irreversible inactivation of I. These ribonucleotide dialdehydes modify the active site of the enzyme, as inclusion of PAPS, or the product, adenosine 3',5'-diphosphate, prevented loss of I activity. p-Nitrophenol did not show similar protective effects. Kinetic studies indicated that the ribonucleotide dialdehydes inactivated the enzyme via a unimol. reaction within a dissociable enzyme-inhibitor complex rather than via a nonspecific bimol. process. Apparently, ribonucleotide dialdehydes are affinity labeling reagents for I, causing enzyme inactivation by the possible formation of a Schiff base adduct with an active-site lysine residue.

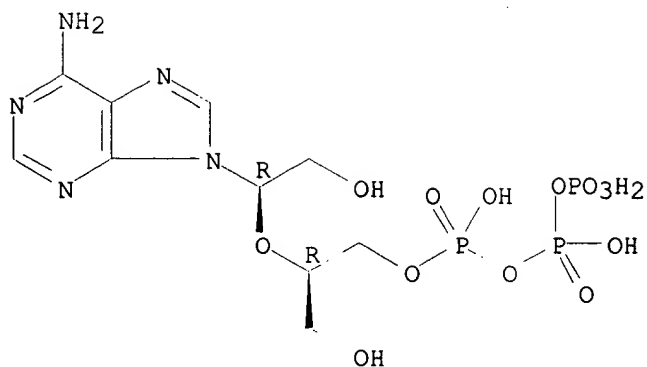
IT 74427-36-4P 84230-56-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 74427-36-4 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

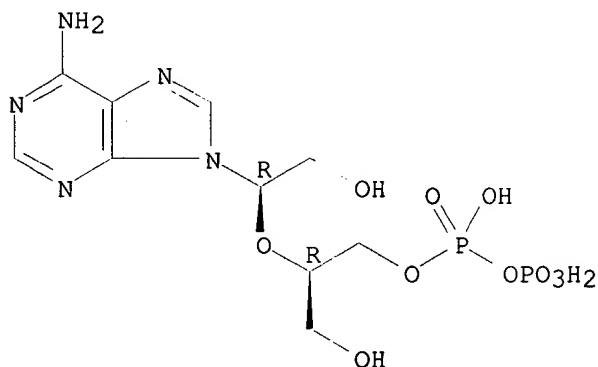
Absolute stereochemistry.



RN 84230-56-8 HCAPLUS

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



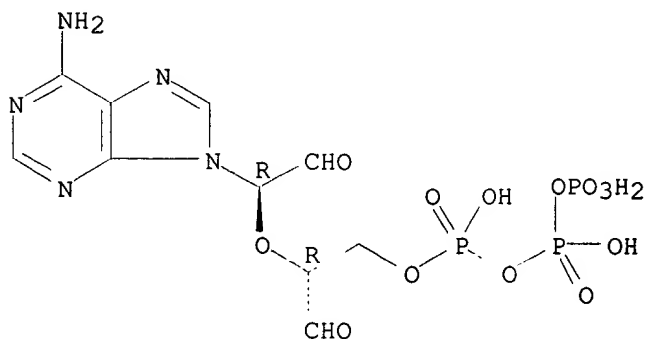
IT 54970-91-1P 64060-84-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and phenol sulfotransferase inhibition by)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



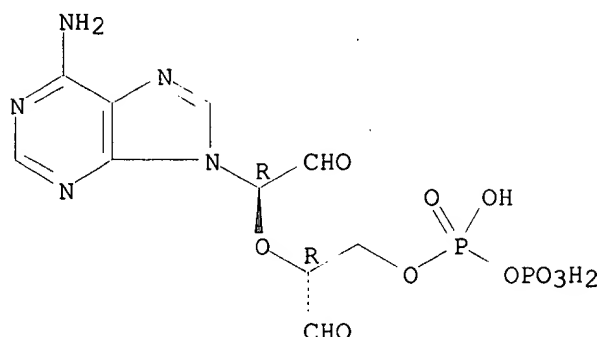
RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-

Searched by: Mary Hale 308-4258 CM-1 12D16

oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 174 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1982:611502 Document No. 97:211502 Photoaffinity labeling of the .beta. subunit of phosphorylase kinase by 8-azidoadenosine 5'-triphosphate and its 2',3'-dialdehyde derivative. King, Marita M.; Carlson, Gerald M.; Haley, Boyd E. (Dep. Chem., Univ. South Florida, Tampa, FL, 33620, USA). J. Biol. Chem., 257(23), 14058-65 (English) 1982. CODEN: JBCHA3. ISSN: 0021-9258.

AB Photoaffinity labeling of rabbit skeletal muscle phosphorylase kinase (I) in the presence of micromolar concns. of [.gamma.-32P]8-azidoadenosine 5'-triphosphate (II) resulted in preferential labeling of its .beta. subunit. Protection from incorporation of II into I was afforded by ADP, ATP, and oATP (ATP 2',3'-dialdehyde). In the presence of Ca²⁺ and Mg²⁺, but in the absence of photolysis, II could be utilized as a substrate for autophosphorylation and phosphorylase conversion, which demonstrated that Mg-II binds to a catalytic site on I. Several effectors, or changes in labeling conditions, strongly influenced affinity labeling of I by II. When photolabeling was carried out with nonactivated I at pH 8.2, or with autophosphorylated enzyme at pH 6.8, 2 conditions known to activate the enzyme, there was a similar decrease in the amt. of labeling. A decrease in labeling was also obsd. in the presence of Ca²⁺ and(or) Mg²⁺. The 2',3'-dialdehyde deriv. of II (III) also preferentially labeled the .beta. subunit of I. In the absence of photolysis, III mimicked previously reported interactions of I with oATP: responsiveness to the synergistic action of Ca²⁺ and Mg²⁺, exhibition of a similar K_i, and the ability to serve as a substrate. Photoincorporation of III showed the same sensitivity toward metal ions that was obsd. with II, and labeling was substantially decreased in the presence of nonradioactive II, suggesting that these 2 analogs may be competing for the same binding site(s).

IT 83700-69-0

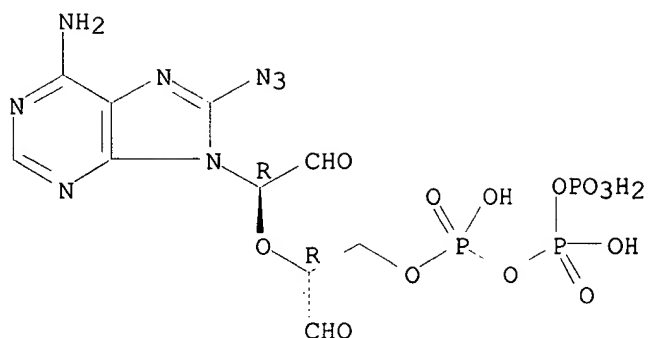
RL: BIOL (Biological study)

(phosphorylase kinase photoaffinity labeling with)

RN 83700-69-0 HCAPLUS

CN Triphosphoric acid, P-[2-[1-(6-amino-8-azido-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 175 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1982:577129 Document No. 97:177129 Catabolic properties of 5',5''-linked dinucleoside phosphates in rat liver nuclei. Bornemann, Siegmund; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Z. Naturforsch., C: Biosci., 37C(9), 818-23 (German) 1982. CODEN: ZNCBDA. ISSN: 0341-0382.

AB The enzymic degrdn. of 14C-labeled 5',5''-linked dinucleoside triphosphates Gp3A, 2-O-methylGp3A, 2'dGp3A, 2',3'-dideoxyGp3A, and 7-methylGp3A in rat liver nuclei was studied. The 2'-deoxy- and 2',3'-dideoxy compds. are poorer substrates than the other cap-structured dinucleotides investigated.

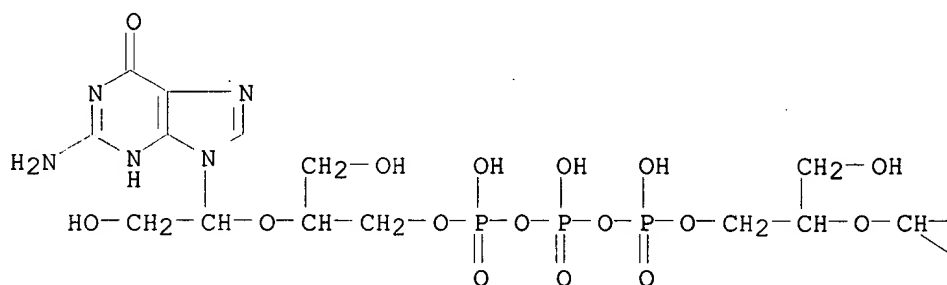
IT 81523-95-7

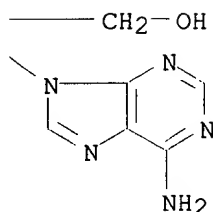
RL: PRP (Properties)
(enzymic degrdn. of, by liver cell nucleus)

RN 81523-95-7 HCAPLUS

CN Triphosphoric acid, P-[2-[1-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] P''-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, stereoisomer (9CI) (CA INDEX NAME)

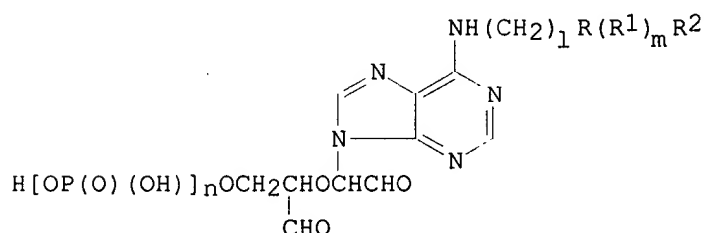
PAGE 1-A





L14 ANSWER 176 OF 233 HCAPLUS COPYRIGHT 2002 ACS
 1982:506259 Document No. 97:106259 Enzyme immobilization. (Unitika Ltd.,
 Japan). Jpn. Kokai Tokkyo Koho JP 57039783 A2 19820305 Showa, 5 pp.
 (Japanese). CODEN: JKXXAF. APPLICATION: JP 1980-115633 19800821.

GI



I

AB A substrate for enzyme immobilization, I, consists of an adenosine deriv. in which R is CONH or CO2, R1 is alkyl, arom., or cycloalkyl, and R2 is a high-mol.-wt. support; l = 1 or 2, m = 0 or 1, and n = 1-3. Thus, 5 g Sepharose 4B was swelled in H2O, activated with CNBr, and suspended in 0.1M NaHSO3. 8-Bromo-N6-carboxyethyl-ADP (200 mg) was added and allowed to react for 12 h at 4.degree.. The gel was then washed, resuspended in 50 mL H2O, and treated with 6 mL 0.5M Na metaperiodate for 1 h at room temp. The treated gel with its ribose 2',3'-dialdehyde deriv. of ADP as a substituent was then washed, suspended in 50 mL 0.1M phosphate buffer, pH 8.5, and mixed with 10 mL of a soln. of Bacillus stearothermophilus acetate kinase in the same buffer. The support immobilized 61,000 of 100,000 units applied; a sample of CH-Sepharose 4B taken for comparison immobilized only 4,000 of 20,000 units applied.

IT 82339-88-6P

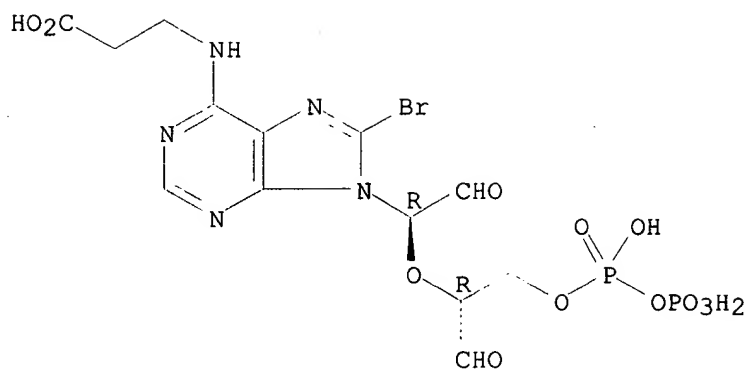
RL: PREP (Preparation)
 (prepn. of, for enzyme immobilization)

RN 82339-88-6 HCAPLUS

CN .beta.-Alanine, N-[8-bromo-9-(1,3-diformyl-6,8,8-trihydroxy-6,8-dioxido-2,5,7-trioxa-6,8-diphosphaoct-1-yl)-9H-purin-6-yl]-, [R-(R*,R*)]- (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



L14 ANSWER 177 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1982:505696 Document No. 97:105696 Nucleotide analogs with modified sugar residues in RNA synthesis by RNA polymerase from *Escherichia coli*. Aivazashvili, V. A.; Bibilashvili, R. Sh.; Florent'ev, V. L. (Inst. Mol. Biol., Moscow, USSR). Mol. Biol. (Moscow), 16(3), 493-8 (Russian) 1982. CODEN: MOBIBO. ISSN: 0026-8984.

AB Triphosphoalkyladenines ppp(CH₂)_nA (I; n = 2-4) and the ATP deriv. (II) inhibited RNA elongation competitively with respect to all 4 natural nucleoside triphosphates, whereas 3'-O-methyl-ATP (III) was a competitive inhibitor only with respect to ATP. I and II were not incorporated into RNA; III was, terminating elongation. The mol. wt. distribution of nascent RNA transcripts of a phage T7 template in the presence of I or II was the same as the normal distribution due to pauses in elongation. This suggests that I and II act by prolonging the natural pauses in RNA formation. This suggestion is supported by the fact that I (n = 3) reduces the rate of chain termination by 3'-O-methyl-GTP. The kinetics of inhibition by I resembled inhibition by inorg. pyrophosphate, which suggests that they interact weakly and reversibly with the substrate-binding site of RNA polymerase.

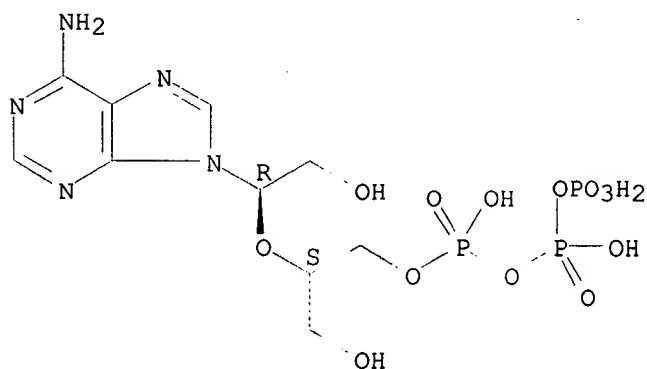
IT 35677-98-6 55881-00-0 55881-01-1
55881-02-2

RL: BIOL (Biological study)
(RNA polymerase inhibition by)

RN 35677-98-6 HCAPLUS

CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

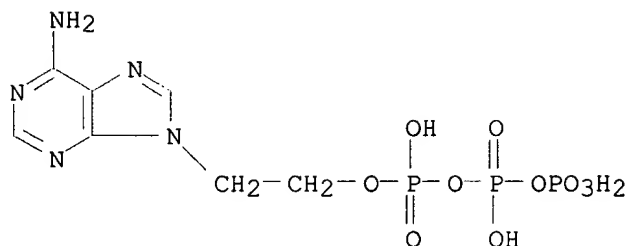
Absolute stereochemistry.



RN 55881-00-0 HCAPLUS

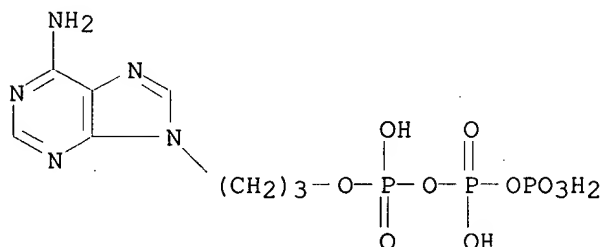
Searched by: Mary Hale 308-4258 CM-1 12D16

CN Triphosphoric acid, P-[2-(6-amino-9H-purin-9-yl)ethyl] ester (9CI) (CA INDEX NAME)



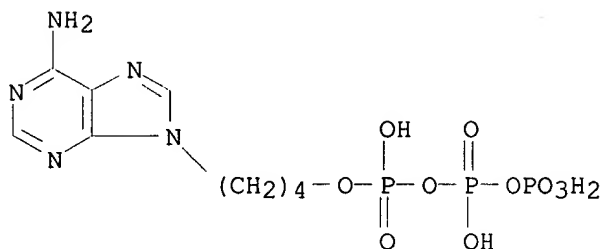
RN 55881-01-1 HCAPLUS

CN Triphosphoric acid, P-[3-(6-amino-9H-purin-9-yl)propyl] ester (9CI) (CA INDEX NAME)



RN 55881-02-2 HCAPLUS

CN Triphosphoric acid, P-[4-(6-amino-9H-purin-9-yl)butyl] ester (9CI) (CA INDEX NAME)



L14 ANSWER 178 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1982:468490 Document No. 97:68490 Interactions between the mitochondrial adenosinetriphosphatase and periodate-oxidized adenosine 5'-triphosphate, an affinity label for adenosine 5'-triphosphate binding sites. Lowe, Peter N.; Beechey, R. Brian (Dep. Biochem., Chelsea Coll., London, SW3 6LX, UK). Biochemistry, 21(17), 4073-82 (English) 1982. CODEN: BICHAW. ISSN: 0006-2960.

AB Periodate-oxidized ATP (I) was prep'd. as an affinity label of nucleotide-binding sites on CHCl3-released ox heart mitochondrial ATPase. In the presence of MgSO4, I is a substrate for the ATPase. It can act as a reversible, competitive inhibitor of ATPase activity and can also induce an irreversible inhibition of ATPase activity. In parallel with the irreversible inhibition, covalent incorporation of [3H]I occurs. ATPase has .apprx.1.05 mol I bound/mol ATPase when the enzyme is 50% inhibited.

Searched by: Mary Hale 308-4258 CM-1 12D16

Most of the covalently bound I is assocd. with the .alpha. and .beta. subunits and is equally distributed between them. The incorporation of I into the ATPase is reduced, and the irreversible inhibition induced by I can be prevented totally by MgADP, MgATP, EDTA/ATP, or EDTA. The location, no., and the functional significance of the I-binding sites are discussed. I can decomp. to form an adenine-contg. compd. and the tripolyphosphate anion in a .beta.-elimination reaction mechanism. The structures of the adenine-contg. compd. and its borohydride redn. product were detd. The adenine-contg. elimination product inhibited the mitochondrial ATPase activity at a rate greater than that obsd. with I. The nature and mechanism of the inhibition of ATPase activity exerted by I and the elimination product were examd. The significance of the .beta.-elimination reaction to the use of periodate-oxidized nucleotides as affinity labels of nucleotide-binding sites on other proteins is discussed.

IT 54970-91-1

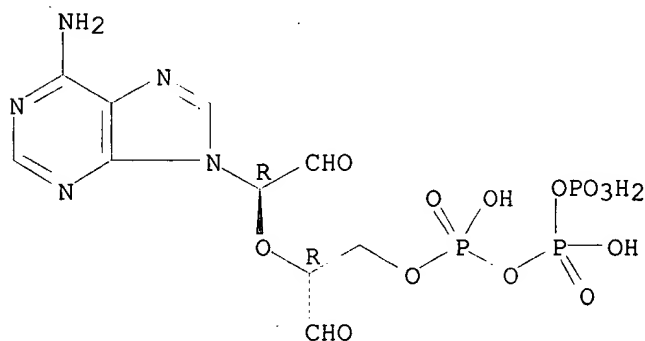
RL: BIOL (Biological study)

(ATPase affinity labeling with, ATP-binding sites in relation to)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 179 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1982:468414 Document No. 97:68414 The reaction of bovine glutamate dehydrogenase with periodate-oxidized ADP. Favilla, Roberto; Bayley, Peter M. (Biophys. Div., Natl. Inst. Med. Res., London, NW7 1AA, UK). Eur. J. Biochem., 125(1), 209-14 (English) 1982. CODEN: EJBCAI. ISSN: 0014-2956.

AB The reactive analog, periodate-oxidized ADP (oADP), was studied as a potential affinity label for bovine glutamate dehydrogenase by using CD difference spectroscopy to monitor specific binding. The analog bound stoichiometrically, rapidly, and reversibly to the adenine nucleotide-binding site with characteristic intensification of the adenine nucleotide CD at 260 nm. This complex was unstable and decayed with a half-life of .apprx.1.5 h; the analog then became attached as a Schiff base to a no. of subsidiary sites, including the enzyme active site, with partial inactivation of the enzyme. Depending upon the initial concn. of oADP, the enzyme activity was progressively lost during the slow reaction; following borohydride redn., .ltoreq.4 mols. of analog were bound/subunit. Protection against loss of enzyme activity was afforded by the coenzyme, NAD, plus glutarate or L-hydroxyglutarate (an effective inhibitor), or by glutarate alone, but not by NAD alone. Spectroscopic and protection studies indicated that after the decay of the specific CD signal, the enzyme retained the capacity to bind ADP, but that this was progressively lost in parallel with the decay of enzyme activity. The results were

consistent with proximity or functional interaction between the adenine nucleotide site and the coenzyme-binding portion of the active site. Thus, oADP does not act as a true affinity label for the adenine nucleotide-binding site, but the reaction subsequent to binding at that site shows some specificity directed toward the active site.

IT **64060-84-0**

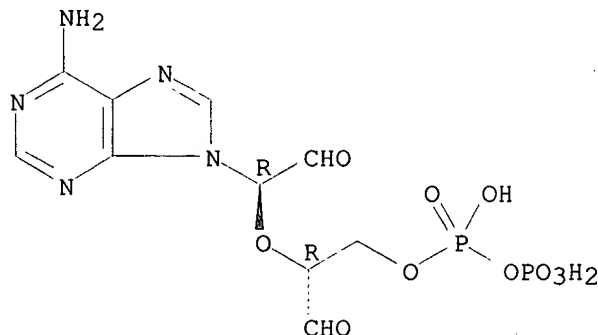
RL: RCT (Reactant)

(reaction of, with glutamate dehydrogenase)

RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 180 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1982:424150 Document No. 97:24150 Preparation, structure, and properties of periodate-oxidized ATP, a potential affinity-labeling reagent. Lowe, Peter N.; Beechey, R. Brian (Dep. Biochem., Chelsea Coll., London, SW3 6LX, UK). Bioorg. Chem., 11(1), 55-71 (English) 1982. CODEN: BOCMBM. ISSN: 0045-2068.

AB Periodate oxidn. of ATP yields a single product which was purified and characterized. Periodate-oxidized ATP (o-ATP) behaves as a single compd. during TLC anal., but NMR spectral studies show that it exists in aq. soln. as an equil. mixt. of 3 dialdehyde monohydrates and a dihydrate. Little free aldehyde is present. The dialdehyde monohydrates are in the form of diastereomeric cyclic hemiacetals. The dialdehyde grouping of o-ATP was reduced with NaBH₄, producing a diol. O-ATP is frequently used in attempts to affinity label nucleotide-binding sites on proteins. The proposed structure of o-ATP is discussed in relation to this use for o-ATP.

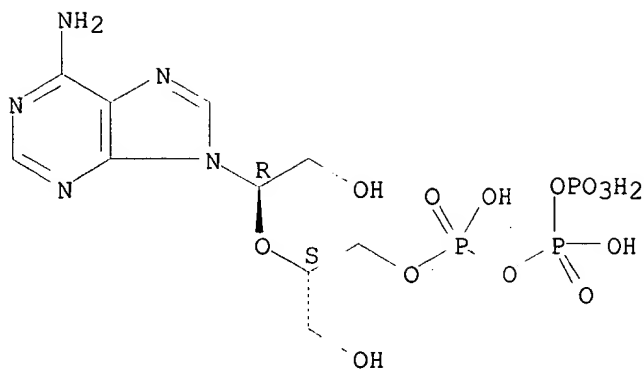
IT **35677-98-6P**

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and NMR of)

RN 35677-98-6 HCAPLUS

CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



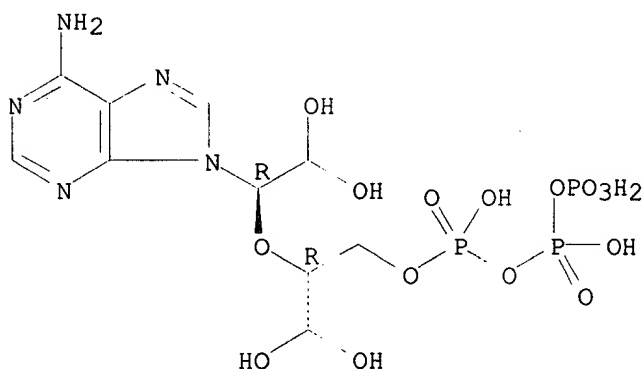
IT 82086-45-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prep. of, by periodate-oxidn. of ATP)

RN 82086-45-1 HCAPLUS

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2,2-dihydroxyethoxy]-3,3-dihydroxypropyl] ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 181 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1982:419816 Document No. 97:19816 Affinity labeling of rabbit muscle pyruvate kinase with dialdehyde-ADP. Hinrichs, Maria Victoria; Eyzaguirre, Jaime (Lab. Bioquim., Univ. Catol., Santiago, Chile). Biochim. Biophys. Acta, 704(2), 177-85 (English) 1982. CODEN: BBACAQ. ISSN: 0006-3002.

AB Periodate-oxidized ADP [dialdehyde-ADP (I)] inactivated rabbit muscle pyruvate kinase (EC 2.7.1.40) II and combined irreversibly with the enzyme. This inactivation was 1st-order with respect to I and followed satn. kinetics, indicating that II 1st forms a reversible complex with the inactivator. Low Mg²⁺ concns. stimulated the rate of inactivation, whereas higher concns. had a protective effect. ADP and ATP, esp. in the presence of Mg²⁺, protected II very strongly against inactivation, whereas phosphoenolpyruvate and pyruvate were less effective. I was not a substrate, but acted as a competitive inhibitor of ADP, with a K_i of 4.5 mM. I had somewhat lower affinity for II than did Mg-ADP, which had a K_d of 1.2 mM. Based on kinetic data, it was shown that 1 mol. of I must combine per enzyme active site in order to inactivate II. Incorporation of I-¹⁴C with the enzyme and treatment of the data by a Tsou plot showed that 6-7 residues/subunit reacted with the modifier, 2 of them being essential for activity. Thus, (1) I behaves as an affinity label of

rabbit muscle II; (2) I probably binds to lysine residues at or near the active site, forming morpholine-like structures; and (3) II possesses 2 modifiable groups essential for activity, the reaction of 1 of them being sufficient to cause total loss of activity.

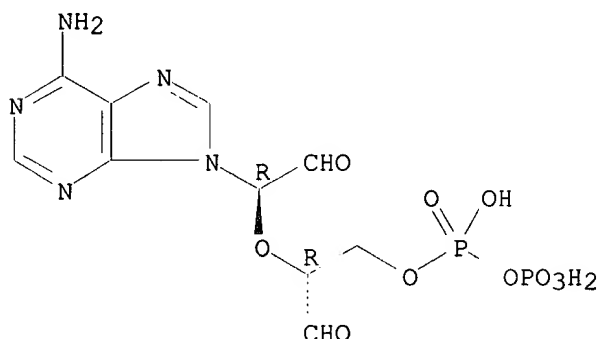
IT 64060-84-0

RL: BIOL (Biological study)
(pyruvate kinase affinity labeling with)

RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 182 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1982:177213 Document No. 96:177213 High-performance liquid-chromatographic method for separation of dinucleotides. Hagemeier, Eberhard; Bornemann, Siegmund; Boos, Karl Siegfried; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). J. Chromatogr., 237(1), 174-7 (English) 1982. CODEN: JOCRAM. ISSN: 0021-9673.

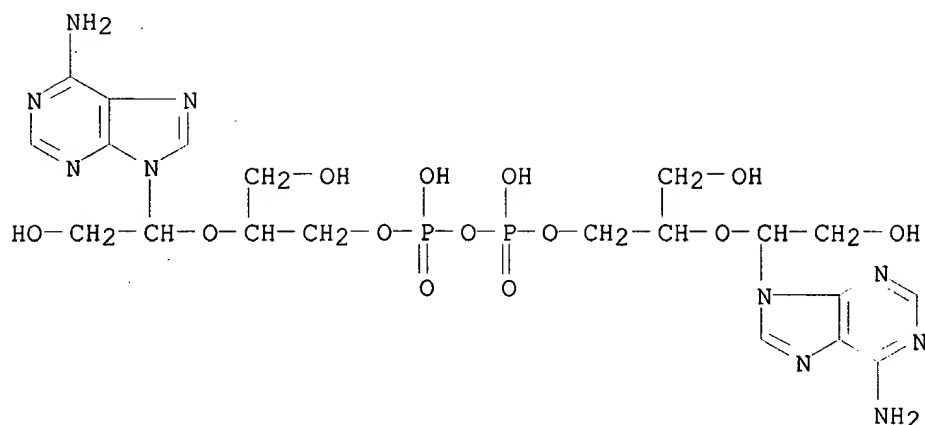
AB Nucleotides were sepd. by high-performance liq. chromatog. (HPLC) at 24.degree. on 2 different systems, and uses of the methods are described for sepg. cap-structured dinucleotides and related compds., monitoring the progress of dinucleotide synthesis, and purity control of naturally occurring and synthesized compds. HPLC was performed on (A) a 300 .times. 2.3 mm column packed with Nucleosil 10 SB (10 .mu.m) or on (B) a 250 .times. 3.2 mm column of Partisil PAC (10 .mu.m). The mobile phase for system A was 0.1M KNO3-0.02M KH2PO4 (pH 2.6), and mobile phases for system B were (B1) 0.8M NH4 formate buffer (pH 4.1), or (B2) 0.4M NH4 formate buffer (pH 4.1), or (B3) a 6- min linear gradient from water up to 0.8M NH4 formate (pH 4.1). Retention times are given for the sepn. of various nucleotides and dinucleoside di-, tri-, tetra-, and pentaphosphates. A very rapid and selective sepn., however, of all nucleotides studied was achieved by the use of system B with linear gradient elution with B3. System A was used to monitor the reaction course of Gp3A synthesis, and system B3 was used to analyze a synthesized Gp3A peak for purity and yield.

IT 81523-93-5 81523-95-7

RL: ANT (Analyte); ANST (Analytical study)
(chromatog. of, high-performance liq.)

RN 81523-93-5 HCAPLUS

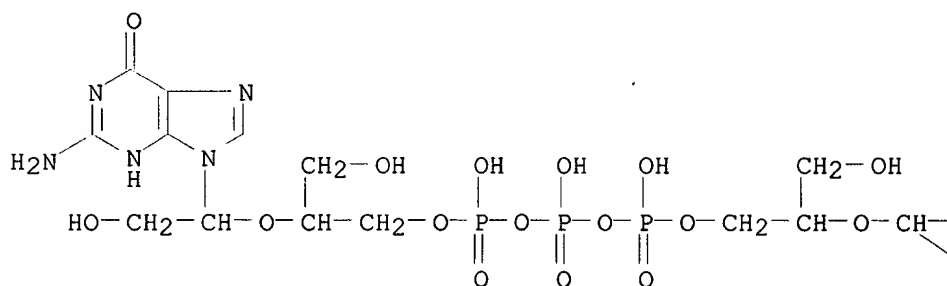
CN Diphosphoric acid, P,P'-bis[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, stereoisomer (9CI) (CA INDEX NAME)



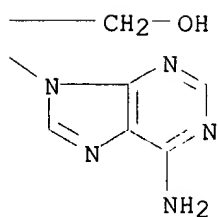
RN 81523-95-7 HCAPLUS

CN Triphosphoric acid, P-[2-[1-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] P'''-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, stereoisomer (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L14 ANSWER 183 OF 233 HCAPLUS COPYRIGHT 2002 ACS
1982:176810 Document No. 96:176810 Irreversible inhibition of adenylate

Searched by: Mary Hale 308-4258 CM-1 12D16

cyclase by oxo-ATP. Skurat, A. V.; Perfileva, E. A.; Khropov, Yu. V.; Bulargina, T. V.; Severin, E. S. (Dep. Biochem., M. V. Lomonosov Moscow State Univ., Moscow, USSR). *Biokhimiya* (Moscow), 47(2), 257-62 (Russian) 1982. CODEN: BIOHAO. ISSN: 0006-307X.

AB Adenylate cyclase from rabbit heart membranes is irreversibly inhibited by the 2',3'-dialdehyde of ATP (oxo-ATP) obtained by periodate oxidn. The inhibiting effect is obsd. during membrane incubation with the inhibitor. NaBH₄ increases the degree of enzyme inactivation by oxo-ATP. Substrate protects the enzyme during incubation of the inhibitor with ATP. Oxo-ATP apparently affects the enzyme active site, blocking the NH₂ group. The rate and equil. consts., k₂ and K_i, for irreversible modification are 0.022 min⁻¹ and 5 .times. 10⁻⁴M, resp.

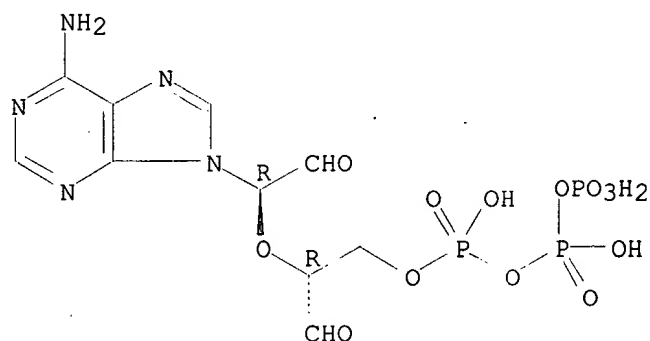
IT 54970-91-1

RL: BIOL (Biological study)
(adenylate cyclase of heart inhibition by)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 184 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1982:64834 Document No. 96:64834 Adenine nucleotide binding sites in normal and mutant adenosine triphosphatases of Escherichia coli. Bragg, Philip D.; Stan-Lotter, Helga; Hou, Cynthia (Dep. Biochem., Univ. British Columbia, Vancouver, BC, V6T 1W5, Can.). *Arch. Biochem. Biophys.*, 213(2), 669-79 (English) 1982. CODEN: ABBIA4. ISSN: 0003-9861.

AB Three types of assays were used to characterize adenine nucleotide binding sites on the Ca²⁺,Mg²⁺-activated ATPase of normal E. coli and its unc A 401 and unc D 412 mutants. ADP was bound mainly at a single site in normal and mutant ATPase. In the absence of divalent cations, ATP was bound at a single high-affinity and 3 low-affinity sites in normal and unc D ATPases. The 2',3'-dialdehyde (oADP) obtained by periodate oxidn. of ADP reacted with both low- and high-affinity sites, whereas oATP (the corresponding dialdehyde of ATP) was bound primarily at a low-affinity site. Two types of adenine nucleotide binding sites, a high-affinity site reacting with ATP and ADP and low-affinity site for ATP, were detected by the effects of these nucleotides on the fluorescence of the aurovertin D-ATPase complex. This high-affinity site(s) was present in normal and mutant ATPases. However, the fluorescence response at both high- and low-affinity sites was modified in the unc D ATPase as a consequence of the abnormal .beta. subunit in this enzyme. Normal fluorescence responses were not induced by the binding of oADP or oATP to the ATPases. ATP was bound at a single site of isolated .alpha. subunits of the enzyme. Since this site was not detected in the unc A ATPase, it is unlikely to be the high-affinity site detected in the intact enzyme or the binding site for the endogenous tightly bound adenine nucleotides found in the purified

ATPase. It is more probable that the site detected on the isolated .alpha. subunit from the normal enzyme is that which binds oADP, as this site was absent in the unc A ATPase. Pretreatment of the normal ATPase with either N,N'-dicyclohexylcarbodiimide (DCCD) or with 4-chloro-7-nitrobenzofurazan (NbfCl), reagents which inhibit ATPase activity by reacting with a .beta. subunit, affected binding of oADP to .alpha. subunit(s) but had less effect with oATP. Inhibition of oADP binding could be due to conformational changes induced in the .alpha. subunit by the reaction of DCCD and NbfCl with a .beta. subunit, or to steric effects. If the latter hypothesis is correct, the active site of the ATPase would be at the interface between .alpha. and .beta. subunits of the enzyme.

IT 54970-91-1 64060-84-0

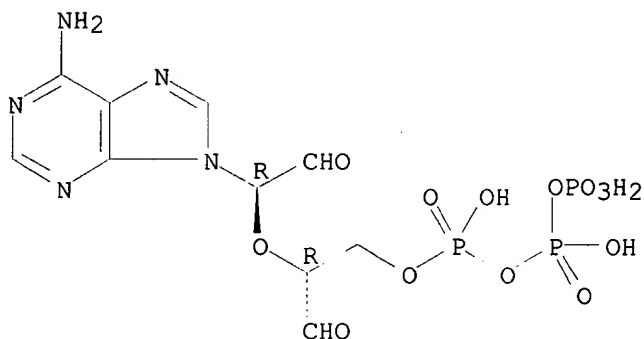
RL: PROC (Process)

(binding of, to normal and mutant ATPase of Escherichia coli)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

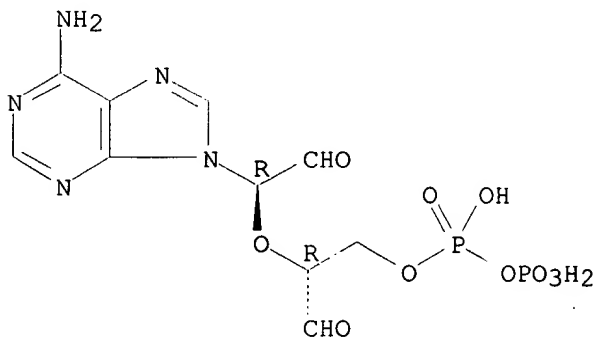
Absolute stereochemistry.



RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 185 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1981:617006 Document No. 95:217006 Specificity in the inactivation of enzymes by periodate-oxidized nucleotides. Mehler, Alan H.; Kim, Jung Ja Park; Olsen, Arne A. (Dep. Biochem., Med. Coll. Wisconsin, Milwaukee, WI, 53226, USA). Arch. Biochem. Biophys., 212(2), 475-82 (English) 1981. CODEN: ABBIA4. ISSN: 0003-9861.

Searched by: Mary Hale 308-4258 CM-1 12D16

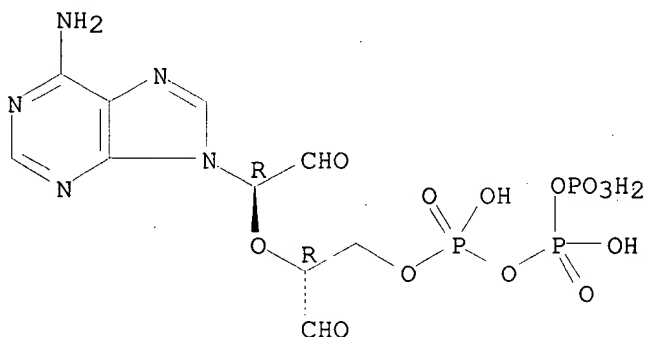
AB Periodate-oxidized ATP (oATP) inactivates the partial reaction of aminoacyl-tRNA synthetases in which the amino acid is transferred to tRNA without altering the other partial reaction in which ATP is a substrate or a product. The inactivation was nonspecific with regard to substituents on the dialdehyde nucleotide (or nucleoside) and with regard to the enzymes susceptible to inactivation. Oxidized GTP and oxidized uridine react as well as oATP with aminoacyl-tRNA synthetases, and all 3 dialdehydes also inactivate rabbit muscle aldolase.

IT **54970-91-1**
 RL: BIOL (Biological study)
 (aminoacyl-tRNA synthetases and aldolase inactivation by)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 186 OF 233 HCAPLUS COPYRIGHT 2002 ACS
 1981:583043 Document No. 95:183043 Photophosphorylation of ribose modified ADP analogs by spinach chloroplasts. Boos, K. S.; Dimke, B.; Schlimme, E.; Wiedner, H.; Edelman, K.; Strotmann, H. (Lab. Biol. Chem., Univ. Paderborn, Paderborn, 4790, Fed. Rep. Ger.). FEBS Lett., 130(1), 73-6 (English) 1981. CODEN: FEBLAL. ISSN: 0014-5793.

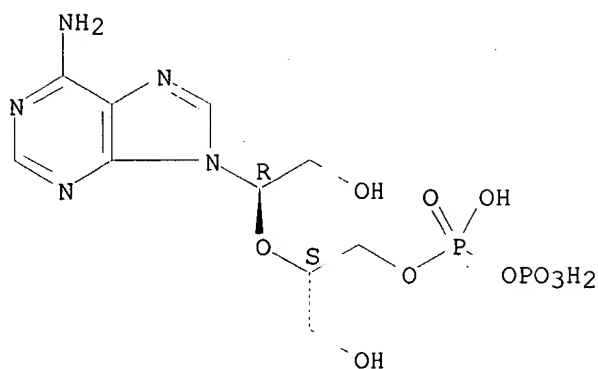
AB The ADP-binding site of chloroplast ATP synthase (I) was mapped by use of ribose-modified ADP analogs. Neither the C2' nor the C3' hydroxyl group was essential for ADP binding and phosphorylation. The results suggested that free rotation of the base around the N-glycosidic linkage as well as rotation around the C4'-C5' bond and pseudorotation of the ribose ring are essential features of the nucleotide mol. with regard to recognition and catalysis by the I active site.

IT **58176-57-1**
 RL: RCT (Reactant)
 (reaction of, with ATP synthetase, structure in relation to)

RN 58176-57-1 HCAPLUS

CN Diphosphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 187 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1981:545941 Document No. 95:145941 Potent inhibition of membrane-bound rat intestinal alkaline phosphatase by a new series of phosphate analogs. Shirazi, Soraya P.; Beechey, R. Brian; Butterworth, Peter J. (Dep. Biochem., Chelsea Coll., London, SW3 6LX, Engl.). Biochem. J., 194(3), 797-802 (English) 1981. CODEN: BIJOAK. ISSN: 0306-3275.

AB Alk. phosphatase (EC 3.1.3.1) of rat intestinal brush-border membrane vesicles was competitively inhibited at pH 7.5 by phenylene-1,3-diphosphonate, 2,6-dinitrophenylphosphonate, and phosphonoacetaldehyde with K_i of 16-80 μM . β -Thio-ADP and γ -thio-ATP were potent, mainly competitive inhibitors ($K_i = 10 \mu\text{M}$) with a slight noncompetitive element. β - γ -Imido-ATP was a competitive inhibitor, but oxidn. of the ribose moiety with NaIO_4 resulted in an active-site-directed irreversible inhibitor that could be of general use in studies of the enzyme mechanism.

IT 78195-29-6

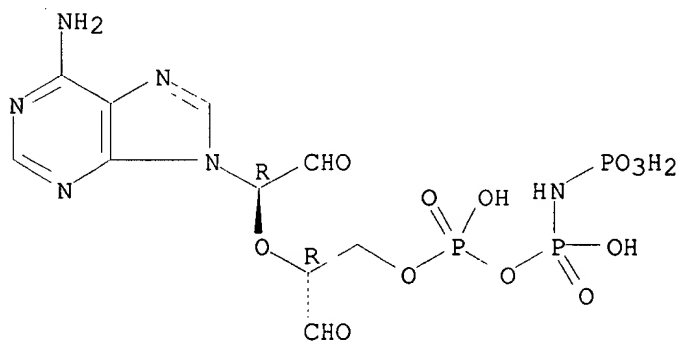
RL: BIOL (Biological study)

(alk. phosphatase of intestinal brush-border membranes inhibition by)

RN 78195-29-6 HCAPLUS

CN Imidotriphosphoric acid, P''-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 188 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1981:457057 Document No. 95:57057 Interaction of phosphorylase kinase with the 2',3'-dialdehyde derivative of adenosine triphosphate. 2. Differential inactivation measured with various protein substrates. King, Marita M.; Carlson, Gerald M. (Dep. Chem., Univ. South Florida, Tampa, FL, 33620, USA). Biochemistry, 20(15), 4387-93 (English) 1981. CODEN:

Searched by: Mary Hale 308-4258 CM-1 12D16

BICHAW. ISSN: 0006-2960.

- AB The 2',3'-dialdehyde deriv. of ATP was used as an affinity label to inactivate phosphorylase kinase in either the presence or absence of Ca^{2+} and Mg^{2+} . Following inactivation, the residual activity of phosphorylase kinase toward various protein substrates was measured and compared with that retained for conversion of phosphorylase b. Three different classes of substrates were distinguished by this anal. For the 1st class (glycogen synthase), inactivation proceeded at the same rate as that measured with phosphorylase conversion, regardless of whether the inactivation was carried out in the presence or absence of the metal ions. For the 2nd class of substrates (troponin I and troponin T), inactivation of the kinase in either the presence or absence of the metals was much more rapid with phosphorylase as substrate. Phosphorylation of the 3rd class of substrates (phosphorylase kinase itself and a synthetic tetradecapeptide) was inactivated in parallel with phosphorylase b when modification was performed in the absence of metals; however, inclusion of Ca^{2+} and Mg^{2+} in the activation mixt. caused activity toward phosphorylase b to be lost more rapidly than that toward the alternative substrates. These results are consistent with a model in which glycogen synthase and phosphorylase b are preferentially phosphorylated at one type of catalytic site in phosphorylase kinase and troponin I and troponin T at another.

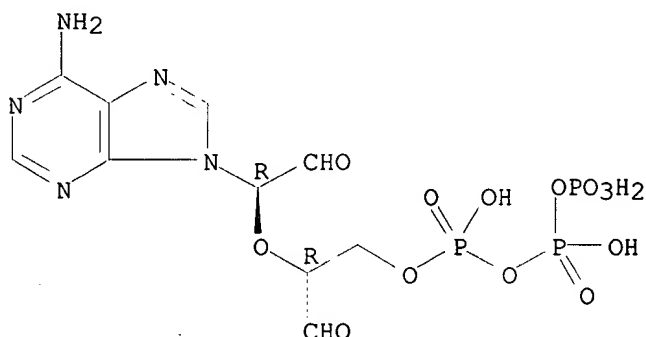
IT 54970-91-1

RL: BIOL (Biological study)
(phosphorylase kinase inactivation by, substrate phosphorylation in relation to)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 189 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1981:457056 Document No. 95:57056 Interaction of phosphorylase kinase with the 2',3'-dialdehyde derivative of adenosine triphosphate. 1. Kinetics of inactivation. King, Marita M.; Carlson, Gerald M. (Dep. Chem., Univ. South Florida, Tampa, FL, 33620, USA). Biochemistry, 20(15), 4382-7 (English) 1981. CODEN: BICHAW. ISSN: 0006-2960.

- AB The 2',3'-dialdehyde deriv. of ATP (oATP) was found to be a valid affinity label for rabbit skeletal muscle phosphorylase kinase. Inactivation by oATP at pH 6.8 followed pseudo-1st-order and satn. kinetics. An apparent K_i of .apprx.6.7 .mu.M was obtained in the presence of 0.6 mM Ca^{2+} plus 10 mM Mg^{2+} . Protection against the rate of inactivation was provided by the natural substrate ATP. In addn., at pH 8.2 oATP could be used as a substrate to phosphorylate phosphorylase b, thus providing evidence that oATP can bind to the active site of phosphorylase kinase. Inactivation of phosphorylase kinase by oATP was sensitive to various effectors of the enzyme such as Ca^{2+} , Mg^{2+} , and pH. Ca^{2+} plus Mg^{2+} synergistically

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enhanced the rate of inactivation several-fold; each metal ion by itself had little effect on the rate of inactivation. This synergism was seen both at pH 6.8 and at pH 8.2; however, the rates of inactivation were much greater at pH 6.8. The enhancement of inactivation by Ca^{2+} plus Mg^{2+} was also more pronounced with activated than with nonactivated kinase.

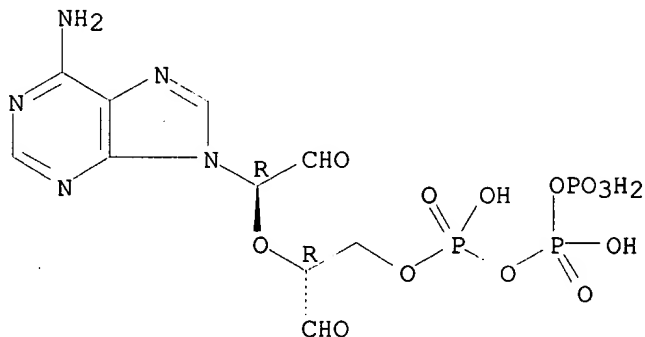
IT 54970-91-1

RL: BIOL (Biological study)
(phosphorylase kinase inactivation by, kinetics of)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



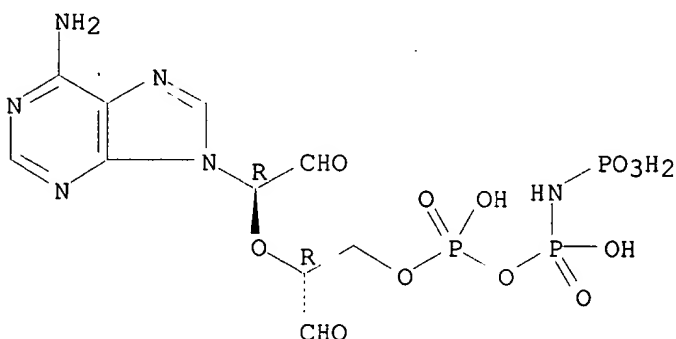
IT 78195-29-6

RL: BIOL (Biological study)
(phosphorylase kinase interaction with)

RN 78195-29-6 HCAPLUS

CN Imidotriphosphoric acid, P''-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 190 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1981:438004 Document No. 95:38004 Competition between ADP and nucleotide analogs to occupy regulatory site(s) related to hysteretic inhibition of mitochondrial F1-ATPase. Baubichon, H.; Godinot, C.; Di Pietro, A.; Gautheron, D. C. (Lab. Biol. Technol., Univ. Claude Bernard Lyon, Villeurbanne, 69622, Fr.). Biochem. Biophys. Res. Commun., 100(3), 1032-8 (English) 1981. CODEN: BBRCA9. ISSN: 0006-291X.

AB The regulatory site(s) responsible for ADP-induced hysteretic inhibition of pig heart mitochondrial F1-ATPase appeared to be specific for adenine nucleotides. The site(s) cannot be readily occupied by guanosine analogs

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IT 64060-84-0

(ATPase F1 inhibition by, regulatory sites in, ADP in relation to)

CN Diposphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Nc1ncnc2c1ncn2N[C@H](C=O)O[C@H](C=O)COP(=O)(O)O

1981:420446 Document No. 95:20446 Phenylalanyl-tRNA synthetase from E. coli MRE-600. Effect of chemical modification of lysine residues on the enzyme interaction with substrates. Gorshkova, I. I.; Datsii, I. I.; Lavrik, O. I.; Nevinskii, G. A. (Inst. Org. Chem., Novosibirsk, USSR). Biokhimiya (Moscow), 46(4), 699-707 (Russian) 1981. CODEN: BIOHAO. ISSN: 0006-307X.

IT 54970-91-1

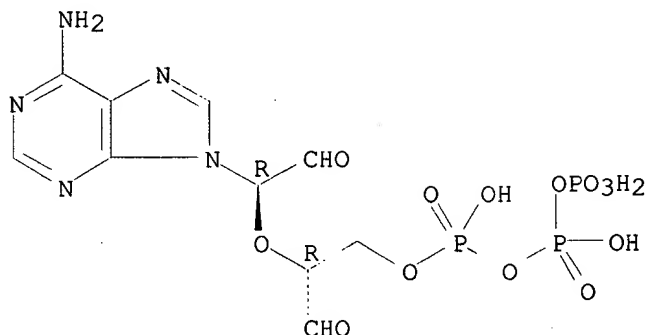
(lysine modification by, in phenylalanyl-tRNA synthetase,

enzyme-substrate interactions in relation to)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 192 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1981:187731 Document No. 94:187731 Affinity labeling of purified calcium-magnesium-activated ATPase of Escherichia coli by the 2',3'-dialdehydes of adenosine 5'-di- and triphosphates. Bragg, Philip D.; Stan-Lotter, Helga; Hou, Cynthia (Dep. Biochem., Univ. British Columbia, Vancouver, BC, V6T 1W5, Can.). Arch. Biochem. Biophys., 207(2), 290-9 (English) 1981. CODEN: ABBIA4. ISSN: 0003-9861.

AB The 2',3'-dialdehydes of ADP and ATP (oADP and oATP, resp.), obtained by periodate oxidn. of ADP and ATP, inhibited the hydrolytic activity of the purified Ca²⁺,Mg²⁺-activated ATPase of E. coli. Nonspecific labeling of amino groups by these dialdehydes was cor. by carrying out the reactions in the presence of 15 mM ATP. Two types of modification of ATP-protectable binding sites by oATP could be detected. The binding of 2 mol ATP-protectable oATP/mol ATPase was without affect on ATPase activity and still occurred in the hydrolytically inactive ATPase of an unCA mutant. The binding of a further 3 mol ATP-protectable oATP/mol ATPase resulted in almost complete loss of ATPase activity although much of the loss occurred during the binding of the 1st addnl. mol. of oATP. This addnl. ATP-protectable oATP binding did not occur in the unCA mutant and so resembled both the inhibitory effect of oADP on the ATPase activity of normal strains and its lack of binding to the unCA ATPase. The ATP-protectable binding sites for oADP and oATP were located on the .alpha. subunit of the ATPase. Binding of oADP or oATP did not result in release of the tightly bound ADP and ATP from the enzyme. Thus, sep. binding sites for oADP and oATP occur on the .alpha. subunits of the E. coli ATPase and the former may be the active site(s) for ATP hydrolysis, whereas the latter are involved in regulation of the ATPase complex.

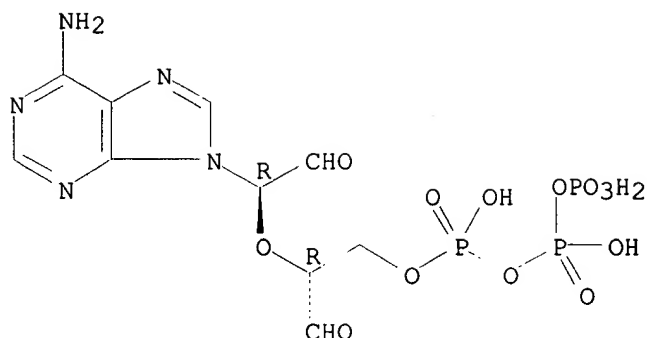
IT 54970-91-1 64060-84-0

RL: BIOL (Biological study)
(ATPase binding sites for)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

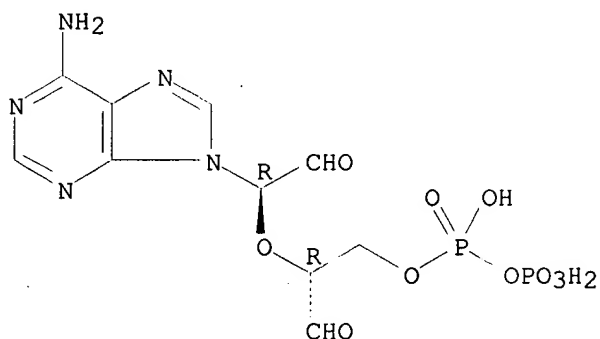
Absolute stereochemistry.



RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 193 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1981:134965 Document No. 94:134965 Interaction of sodium, potassium ATPase with modifying ATP analogs and chloromethylphosphonic acid. Mirsalikhova, N. M.; Baranova, L. A.; Tunitskaya, V. L.; Gulyaev, N. N. (Dep. Biochem., Moscow State Univ., Moscow, USSR). Biokhimiya (Moscow), 46(2), 314-26 (Russian) 1981. CODEN: BIOHAO. ISSN: 0006-307X.

AB The interaction of synthetic ATP analogs, contg. active groups in the triphosphate moiety and in the 8-position of the nucleotide moiety, with highly purified Na⁺, K⁺-ATPase from the medullar layer of porcine kidney was studied. Eleven out of 17 ATP analogs studied irreversibly inhibited the ATPase activity of the enzyme. The pH optimum of the enzyme inactivation by adenosine-5'-(.beta.-chloroethylphosphate) and adenosine-5'-(p-fluorosulfonylphenylphosphate) in addn. to the pronounced protective effect of ATP suggests possible covalent blocking of histidine and dicarboxylic amino acid residues in the enzyme active center. The irreversible inhibition of the enzyme by oxo-ATP, contg. aldehyde groups in the modified ribose residue in the presence of NaBH₄, suggests a possible presence of a lysine residue .epsilonpsilon.-amino group in the ATP-binding site of the enzyme. Na⁺, K⁺-ATPase possesses an inorg. phosphate-binding site, which is specifically blocked by chloromethylphosphonic acid. The accessibility of this site for modification depends on ATP, Na⁺, and K⁺.

IT 54970-91-1

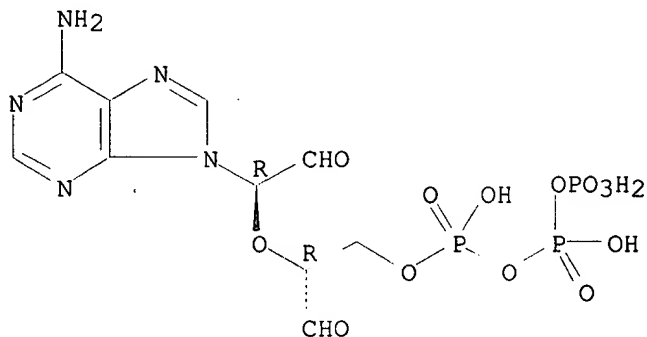
RL: BIOL (Biological study)
(ATPase of kidney inactivation by)

RN 54970-91-1 HCAPLUS

Searched by: Mary Hale 308-4258 CM-1 12D16

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 194 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1980:633925 Document No. 93:233925 Dissection of the active site of rabbit liver tRNA nucleotidyltransferase. Specificity and properties of subsites for donor nucleoside triphosphates. Masiakowski, Piotr; Deutscher, Murray P. (Dep. Biochem., Univ. Connecticut Health Cent., Farmington, CT, 06032, USA). J. Biol. Chem., 255(23), 11240-6 (English) 1980. CODEN: JBCHA3. ISSN: 0021-9258.

AB tRNA nucleotidyltransferase (I) incorporates both AMP and CMP into tRNA acceptors. Studies of the effects of nucleoside triphosphates, nucleotide analogs, and affinity reagents on AMP and CMP incorporation indicate that these residues are donated from different subsites. However, neither of these sites is completely specific for nucleoside triphosphate binding, and CMP can actually be incorporated from the AMP-donating site, although at a slow rate. The 2 donor subsites interact with each other, such that binding of a ligand to the ATP site stimulates incorporation from the CMP-donating site. This interaction accounts for the biphasic CTP satn. curve and the unusual effects of nucleoside triphosphates on CMP incorporation obsd. earlier. In addn. to donating CMP, the CTP subsite also serves as the position of binding of the terminal cytidine residue of tRNA-C-C and, in the absence of CTP, for binding of the terminal residue of tRNA-C. These results have defined multiple accepting and donating subsites within the active site of tRNA nucleotidyltransferase, as predicted from a previous model for enzyme action. However, since definitive evidence for 2 CMP-donating sites was not obtained, a modification of this earlier model which utilizes only a single CMP-donating site was considered. Using these models, the specificity of the donor and acceptor subsites in relation to the accurate synthesis of the -C-C-A sequences of tRNA is discussed.

IT 54970-91-1

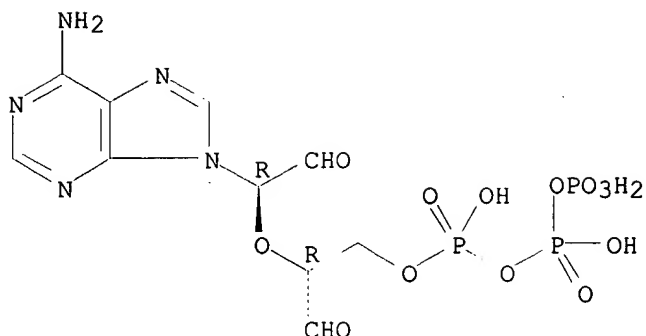
RL: BIOL (Biological study)

(transfer RNA nucleotidyltransferase affinity modification by)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 195 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1980:617110 Document No. 93:217110 Simple immobilization method for NAD(+) with the preservation of coenzyme activity. Schoepp, W.; Lorenz, Rita (Ber. Biochem., Karl-Marx-Univ. Leipzig, Leipzig, 7010, Ger. Dem. Rep.). Acta Biol. Med. Ger., 39(2-3), 335-7 (German) 1980. CODEN: ABMGJ. ISSN: 0001-5318.

AB NAD was oxidized by periodate and immobilized on an adipic acid dihydrazide-Sepharose 4B conjugate by means of the aldehyde groups formed. The substitution degree of the NAD-Sepharose was between 0.26 and 0.82 .mu.mol NAD/mL Sepharose gel. At least 90% of the immobilized NAD could be reduced by NaBH4. The immobilized coenzyme was active in the reaction with alc. dehydrogenase and EtOH; .apprx.30% of the coenzyme was reduced in the enzymic reaction at pH 8.0 in 0.067M phosphate buffer. The immobilized coenzyme prepn. is relatively sensitive to hydrolysis; after 14 days storage in water at 4.degree., the enzymically reducible portion of coenzyme was decreased to 50% the original value.

IT 75521-15-2DP, Sepharose deriv.

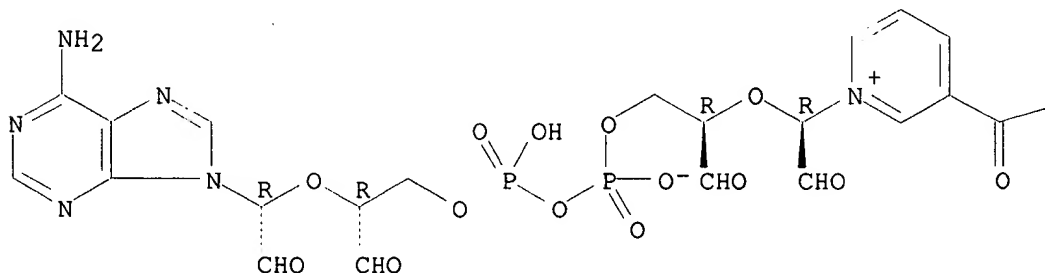
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction with alc. dehydrogenase)

RN 75521-15-2 HCAPLUS

CN Pyridinium, 3-(aminocarbonyl)-1-[13-(6-amino-9H-purin-9-yl)-1,3,11,13-tetraformyl-6,8-dihydroxy-6,8-dioxido-2,5,7,9,12-pentaoxa-6,8-diphosphatridec-1-yl]-, inner salt, [1R-(1R*,3R*,11R*,13R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



—NH₂

L14 ANSWER 196 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1980:581871 Document No. 93:181871 Inhibition of adenylate cyclase by the 2',3'-dialdehyde of adenosine triphosphate. Westcott, Keith R.; Olwin, Bradley B.; Storm, Daniel R. (Dep. Pharmacol., Univ. Washington, Seattle, WA, 98195, USA). J. Biol. Chem., 255(18), 8767-71 (English) 1980. CODEN: JBCHA3. ISSN: 0021-9258.

AB The periodate-oxidized analog of ATP, ATP-2',3'-dialdehyde (I), competitively inhibited bovine brain and rat liver adenylate cyclase (II). The apparent K_i for inhibition of brain II by I was 196 .mu.M in the presence of Mg²⁺ and 37 .mu.M in the presence of Mn²⁺. The K_i values for inhibition of rat liver II by I were 48 and 30 .mu.M in the presence of Mg²⁺; and Mn²⁺, resp. II activity was irreversibly inactivated by I in the presence of NaCNBH₃ and the kinetics for loss in enzyme activity were pseudo-1st order. Both ATP and Tris protected II from irreversible inhibition by I and NaCNBH₃. Apparently, I forms a Schiff base with an amino group at the active site of the enzyme and NaCNBH₃ redn. of this Schiff base causes irreversible modification of the catalytic subunit. The K_m for I inactivation, and protection of the enzyme by ATP were not affected by the presence or absence of free Mg²⁺. These data indicate that a divalent cation is not required for binding of I to the active site of II.

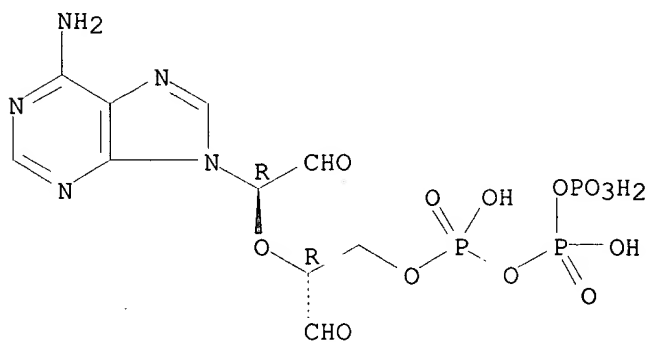
IT 54970-91-1

RL: BIOL (Biological study)
(adenylate cyclase inhibition by, kinetics of)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 197 OF 233 HCAPLUS COPYRIGHT 2002 ACS

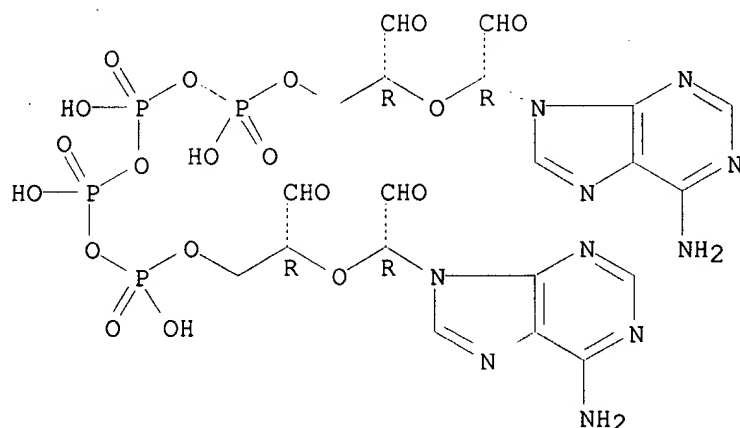
1980:565266 Document No. 93:165266 Intracellular signals of proliferation control: diadenosine tetraphosphate (Ap₄A) - a trigger of DNA replication. Grummt, F. (Max-Planck-Inst. Biochem., Munich, D-8033, Fed. Rep. Ger.). Control Mech. Anim. Cells: Specific Growth Factors, [Pap. Round Table], Meeting Date 1979, 109-19. Editor(s): Jimenez de Asua, Luis; Levi-Montalcini, Rita; Shields, Robert. Raven: New York, N. Y.

Searched by: Mary Hale 308-4258 CM-1 12D16

(English) 1980. CODEN: 43WHA2.

- AB Diadenosine tetraphosphate (Ap4A) was able to induce DNA replication in G1-arrested BHK cells in vitro and was bound to the 57,000-dalton subunit of DNA polymerase .alpha. (I) in a dose-dependent manner. The covalent binding of oxidized Ap4A to I inactivated the enzyme. The capability of rat cerebral neurons to bind Ap4A declined during development (5 days before to 60 days after birth) with a similar rate as did the I activity, indicating a specific correlation between the level of replicating activity and the Ap4A-binding capacity in neuronal cells. Methylene-bis-ADP(II), a structural analog of Ap4A, competed at a 1:1 ratio with Ap4A for its binding site at I. Methylene-bis-AMP was inactive, whereas ADP competed only at a 100-fold excess with Ap4A for its binding site. DNA synthesis in vitro was strongly inhibited by II. In both 3T3 and SV40-transformed 3T3, methylene-bis-5'-AMP inhibited in vivo DNA synthesis from [3H]thymidine. The addn. of methylene-bis-adenosine to the cultures not only completely inhibited DNA replication but also the proliferation of these cells.
- IT **75042-77-2**
RL: BIOL (Biological study)
(DNA polymerase .alpha. inhibition by)
- RN 75042-77-2 HCAPLUS
- CN Tetraphosphoric acid, P,P'''-bis[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, [2R-[1[R*(R*)],2R*(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 198 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1980:563484 Document No. 93:163484 A difference in the affinity labeling of calcium, magnesium-activated ATPases of normal and unc A strains of Escherichia coli by the 2',3'-dialdehyde derivative of adenosine 5'-diphosphate. Bragg, P. D.; Hou, C. (Dep. Biochem., Univ. British Columbia, Vancouver, BC, V6T 1W5, Can.). Biochem. Biophys. Res. Commun., 95(3), 952-7 (English) 1980. CODEN: BBRC9. ISSN: 0006-291X.

- AB The 2',3'-dialdehyde of ADP, obtained by IO4- oxidn. of ADP, inhibited the hydrolytic activity of the purified Ca2+,Mg2+-activated ATPase of Escherichia coli. In the initial stages of the reaction, inhibition was due to the reaction of 1 mol inhibitor/active site. When nonspecific labeling of amino groups by the dialdehyde was lowered by the simultaneous presence of 15 mM ATP in the reaction mixt., 3 mol ATP-protectable binding sites/mol ATPase were found. ATP-protectable binding of the dialdehyde was not obsd. when the hydrolytically inactive ATPase of an unc A mutant of E. coli was used, although binding of the inhibitor to nonprotected amino groups still occurred. This suggests that the mutant ATPase is unable to bind ATP or that the amino groups with which the dialdehyde

reacts in the native enzyme are absent or masked.

IT 64060-84-0

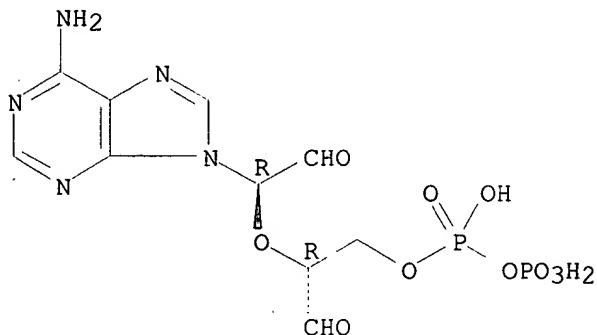
RL: BIOL (Biological study)

(ATPase of Escherichia normal and mutant strains affinity labeling by, ATP effect on)

RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 199 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1980:463716 Document No. 93:63716 On the chemical communication between the mitochondrial adenine nucleotide carrier and its substrate. Schlimme, Eckhard; Boos, Karl Siegfried; De Groot, Egon Jabbo (Lab. Biol. Chem. Fachber. Naturwiss., Univ. Paderborn, Paderborn, Fed. Rep. Ger.). Mol. Mech. Biol. Recognition, Proc. Aharon Katzir-Katchalsky Conf., Meeting Date 1978, 443-8. Editor(s): Balaban, Miriam. Elsevier: Amsterdam, Neth. (English) 1979. CODEN: 43GWAZ.

AB The effect of base, sugar, or phosphate group modification of adenine nucleotides on the carrier protein-mediated translocation mechanism were studied to elucidate the structural requirements of the adenine nucleotide which are essential for recognition by the membrane-bound receptor (carrier-specific binding) and addnl. required to trigger the transfer. Structural modifications of the adenine base were tolerated by the adenine nucleotide carrier, an integral lipoprotein of the inner mitochondrial membrane, with respect to binding and exchange, provided that the electron distributions in the heterocycle, including an unmodified C6-amino group, were retained, i.e. the adenine character of the base remained unchanged. Modification of the phosphate chain had only moderate influence on carrier-specific binding and exchange, provided that the no. of neg. charges in the phosphate chain was unchanged. Modified nucleotide substrates with a conformation equiv. to that of ATP (anti, gauche, gauche) could not be accommodated in the carrier binding site and the transfer did not occur. The D-configuration of the ribose had to remain unchanged; no inversion of chirality was tolerated by the carrier with the exception of the 3'-hydroxyl group which could be substituted by H. The 2'-hydroxyl group was necessary for the bound nucleotide to trigger the transmembrane adenine nucleotide exchange.

IT 74427-36-4

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(adenine nucleotide carrier of mitochondria specificity for)

RN 74427-36-4 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

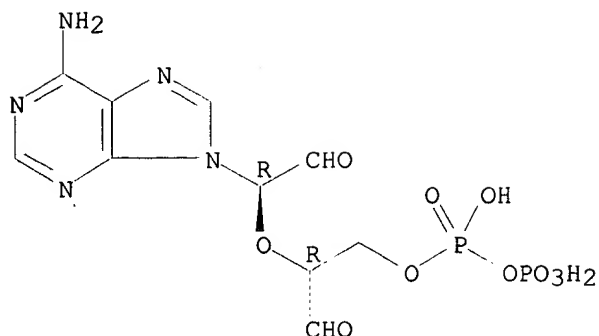
Nc1nc2nc(NC[C@H](O)[C@@H](O)COP(=O)(O)OP(=O)(O)O)cnc2n1

1980:440446 Document No. 93:40446 The non-catalytic nucleotide-binding site of mitochondrial ATPase is localized on the .alpha.-subunit(s) of factor F1. Kozlov, I. A.; Mil'grom, Ya. M. (Isotope Dep., Moscow State Univ., Moscow, 117234, USSR). Eur. J. Biochem., 106(2), 457-62 (English) 1980. CODEN: EJBCAI. ISSN: 0014-2956.

IT 64060-84-0
RL: PROC (Process)
(ATPase .alpha.-subunit binding of)

CN Diposphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Searched by: Mary Hale 308-4258 CM-1 12D16



L14 ANSWER 201 OF 233 HCAPLUS COPYRIGHT 2002 ACS
 1980:439691 Document No. 93:39691 P1,P3-[5'-guanosyl-5''-[14C]-adenosyl]triphosphate: preparation of the cap parent compound and its catabolism by rat liver subcellular fractions. Bornemann, Siegmund; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Gesamthochsch. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Z. Naturforsch., C: Biosci., 35C(1-2), 57-64 (German) 1980. CODEN: ZNCBDA. ISSN: 0341-0382.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The chem. synthesis of P1,P3-(5'-guanosyl-5''-[14C]adenosyl)triphosphate (labeled I), which is the labeled parent compd. of 5'-terminal cap structures of most eukaryotic mRNA's, as well as of noncap structures and derivs. is described. I and the noncap-structured nucleotide Ap2A-14C (II), as well as their labeled ribose-ring-opened derivs., III and IV, resp., were incubated with rat liver nuclei, mitochondria, and other subcellular fractions. The nucleases present in the nuclear fraction preferentially degraded I over the other structures, whereas there was no such preference in degrdn. by mitochondria, 500 g supernatant (homogenate minus nuclei), or 15,000 g supernatant. Evidently, cap-degrading nucleases able to unblock 5'-termini of mRNA are present in liver nuclei but not mitochondria. Also, an intact ribofuranoside system in the dinucleoside triphosphates is apparently required by the cap-degrading nucleases.

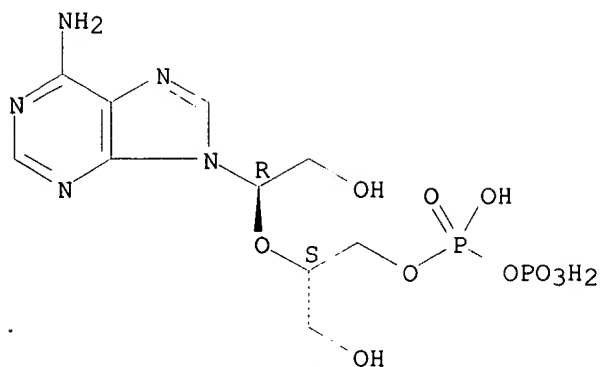
IT 73566-18-4P

RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
 (formation of, from P1,P3-guanosyladenosyl triphosphate ribose-ring-opened deriv.)

RN 73566-18-4 HCAPLUS

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, labeled with carbon-14, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



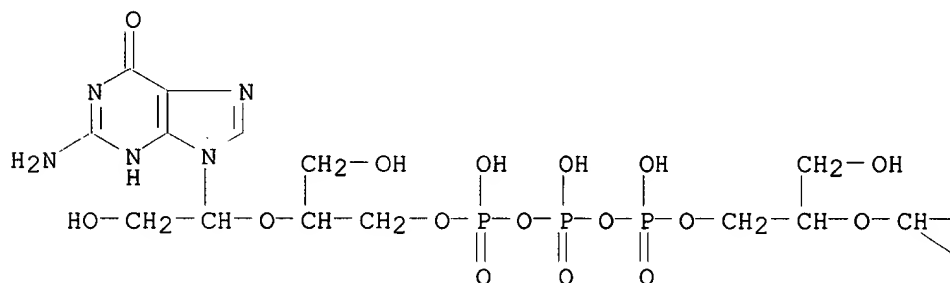
IT 73566-13-9P 73566-15-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and degrdn. by nucleases)

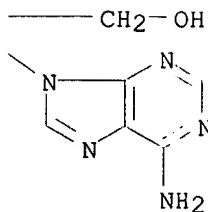
RN 73566-13-9 HCAPLUS

CN Triphosphoric acid, P-[2-[1-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] P''-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, labeled with carbon-14, stereoisomer (9CI) (CA INDEX NAME)

PAGE 1-A



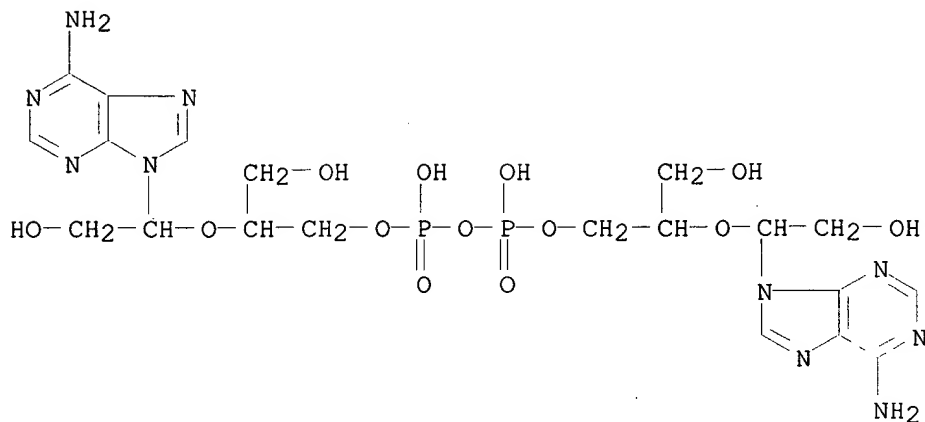
PAGE 1-B



RN 73566-15-1 HCAPLUS

Searched by: Mary Hale 308-4258 CM-1 12D16

CN Diphosphoric acid, P,P'-bis[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, labeled with carbon-14, stereoisomer (9CI) (CA INDEX NAME)



L14 ANSWER 202 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1980:76842 Document No. 92:76842 Synthesis and circular dichroism spectra of dinucleoside phosphate analogs containing 1-(.beta.-hydroxyethoxymethyl)cytosine and 9-(.beta.-hydroxyethoxymethyl)adenine. Tychinskaya, L. Yu.; Lysov, Yu. P.; Florent'ev, V. L. (Inst. Mol. Biol., Moscow, USSR). Bioorg. Khim., 5(7), 1059-70 (Russian) 1979. CODEN: BIKHD7.

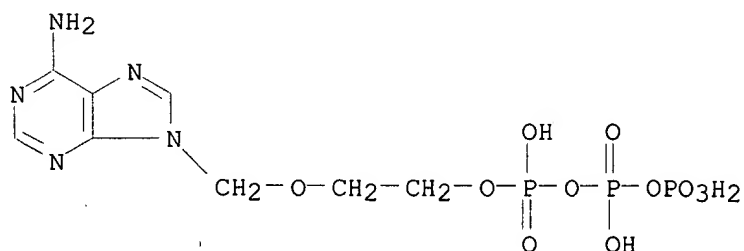
AB Analogs of dinucleoside phosphates were synthesized contg. 1-(2-hydroxyethoxymethyl)cytosine (CytMeOEtOH) and 9-(2-hydroxyethoxymethyl)adenine (AdeMeOEtOH) either at the 3'- or 5'-end, e.g. AdeMeOEtO-P-Ado (Ado = adenosine), Ado-P OEtOMeAde, CytMeOEtO-P-Ado, Cyd-P-OEtOMeAde, or Ado-P-OEtOMeCyt. Addnl. mono- and triphosphates of CytMeOEtOH and AdeMeOEtOH were prepd. The temp. dependence of CD spectra of dinucleoside phosphate analogs was examd. (0.1M phosphate buffer, pH 7; 6.4M LiCl) and thermodyn. parameters for the equil. described by a 2-state model were detd. The contribution of the ether O of the ribose ring to the organization and stabilization of the single-stranded helix of oligonucleotides was discussed.

IT 72710-15-7

RL: PRP (Properties)
(NMR and UV spectrum of)

RN 72710-15-7 HCAPLUS

CN Triphosphoric acid, P-[2-[(6-amino-9H-purin-9-yl)methoxy]ethyl] ester (9CI) (CA INDEX NAME)



L14 ANSWER 203 OF 233 HCAPLUS COPYRIGHT 2002 ACS

Searched by: Mary Hale 308-4258 CM-1 12D16

1980:1735 Document No. 92:1735 Mitochondrial adenine nucleotide carrier. Investigation of principal structural, steric, and contact requirements for substrate binding and transport by means of ribose-modified substrate analogs. Boos, Karl Siegfried; Schlimme, Eckhard (Lab. Biol. Chem., Univ. Paderborn, Paderborn, D-4790, Fed. Rep. Ger.). Biochemistry, 18(24), 5304-9 (English) 1979. CODEN: BICHAW. ISSN: 0006-2960.

AB A selected series of 14 ribose-modified adenine nucleotide analogs was prepd. and characterized as the .alpha.-32P- or U-14C-labeled compds. The capacity of rat liver mitochondria for adenine nucleotide carrier-linked (specific) binding and carrier-mediated transfer across the inner mitochondrial membrane as well as the amt. of noncarrier-linked (unspecific) binding of these analogs was detd. at 5.degree. by an inhibitor (atractyloside) stop-method and compared with these values with the natural substrates ADP and ATP. Kinetic data of carrier-specific bound analogs were evaluated from Dixon plots and indicate that these analogs act as competitive inhibitors for mitochondrial ADP and ATP uptake. The findings confirm the distinct substrate specificity of the carrier system. By use of the analogs, an exptl. proof of the 2-step nature of mitochondrial adenine nucleotide translocation, i.e., carrier-specific binding (recognition) and transport, was obtained. Furthermore, the findings provide a detailed description of the basic steric, contact, and structural elements which are prerequisite for carrier-specific binding (A) and addnl. for subsequent transport (B): (A) (1) an anti- or syn-positioned .beta.-N-glycosyl-linked purine base; (2) an S- or N-type sugar pucker; (3) a cis disposition of the C(4')-C(5') bond with respect to the heterocycle; (B) (1) a nonfixed anti-positioned purine base with a N-glycosyl torsion angle of .apprx.-20.degree.; (2) an S-type sugar pucker; (3) a gauche-gauche orientation of the exocyclic C(5')-O(5') group; and (4) a trans-positioned [C(2') ribo] hydroxyl group, which presumably triggers the induction of carrier-mediated transport.

IT 71997-39-2 71997-40-5 71997-42-7

71997-43-8

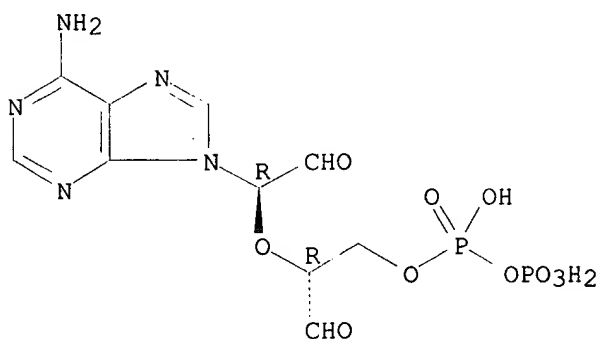
RL: BIOL (Biological study)

(adenine nucleotide carrier of mitochondria interaction with)

RN 71997-39-2 HCAPLUS

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, disodium salt, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



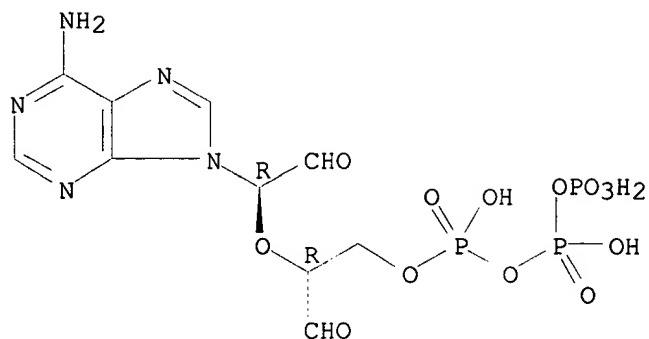
● 2 Na

RN 71997-40-5 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester, trisodium salt (9CI) (CA INDEX NAME)

Searched by: Mary Hale 308-4258 CM-1 12D16

Absolute stereochemistry.

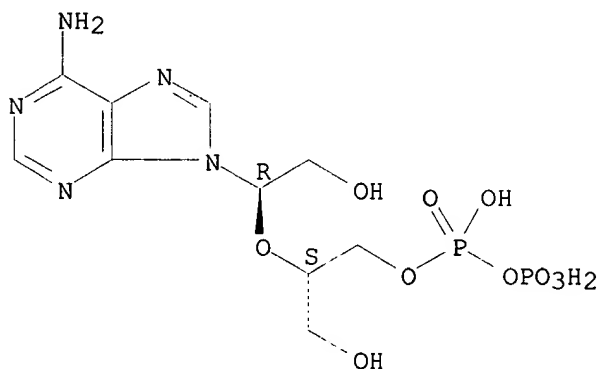


● 3 Na

RN 71997-42-7 HCAPLUS

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, disodium salt, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

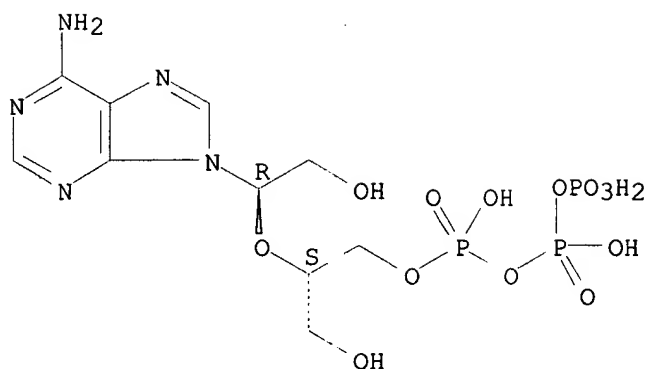


● 2 Na

RN 71997-43-8 HCAPLUS

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester, trisodium salt, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●3 Na

L14 ANSWER 204 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1979:519380 Document No. 91:119380 Inactivation of phosphofructokinase by dialdehyde-ATP. Gregory, Martha R.; Kaiser, E. T. (Dep. Chem., Univ. Chicago, Chicago, IL, 60637, USA). Arch. Biochem. Biophys., 196(1), 199-208 (English) 1979. CODEN: ABBIA4. ISSN: 0003-9861.

AB Rabbit muscle phosphofructokinase (PFK) was rapidly inactivated by a 2',3'-dialdehyde deriv. of ATP. When allowed to react with 0.6 mM dialdehyde-ATP in 0.1M borate buffer (pH 8.6) contg. 0.2 mM EDTA and 0.5 mM dithiothreitol, PFK lost essentially all activity (99%) in 30 min. The modified PFK remained inactive following dialysis of the reaction mixt. against Na borate (pH 8.0) contg. fructose diphosphate, EDTA, and dithiothreitol. Expts. with ¹⁴C-labeled dialdehyde-ATP showed that 99% inactivation of PFK corresponds to incorporation of 3-4 mol of the ATP analog/PFK protomer. The inactivation of PFK with dialdehyde reagent was not caused by disocn. of the 340,000 mol. wt. tetramer to the 170,000 mol. wt. dimer, as detd. by anal. ultracentrifugation. ADP or ATP protected PFK from inactivation by dialdehyde-ATP at pH 8.6, but fructose 6-phosphate, cyclic AMP, or fructose diphosphate, which protect PFK from modification by pyridoxal phosphate, provided little protection from inactivation. Amino acid analyses of dialdehyde-inactivated PFK and of a control sample of the enzyme were compared following reaction of each with 2,4-dinitrofluorobenzene. Three or 4 lysine residues/PFK protomer were modified by dialdehyde-ATP. These lysine residues react with dialdehyde-ATP to form dihydroxymorpholine-like adducts rather than Schiff bases.

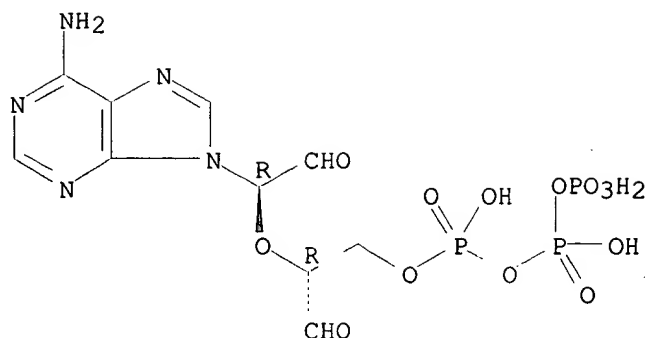
IT 54970-91-1

RL: BIOL (Biological study)
(phosphofructokinase inactivation by)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 205 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1979:486450 Document No. 91:86450 Yeast phenylalanyl-tRNA synthetase. Affinity and photoaffinity labeling of the stereospecific binding sites. Baltzinger, Mireille; Fasiolo, Franco; Remy, Pierre (Inst. Biol. Mol. Cell., CNRS, Strasbourg, Fr.). Eur. J. Biochem., 97(2), 481-94 (English) 1979. CODEN: EJBCAI. ISSN: 0014-2956.

AB The localization of the binding sites of the different ligands on the constitutive subunits of yeast phenylalanyl-tRNA synthetase (I) was undertaken using a large variety of affinity and photoaffinity labeling techniques. The tRNA^{Phe} was crosslinked to I by nonspecific UV irradiation at 248 nm, specific irradiation in the Y base absorption band (315 nm), irradiation at 335 nm, in the absorption band of 4-thiouridine residues introduced in the tRNA molecule, or by Schiff base formation between periodate-oxidized tRNA^{Phe} (tRNA^{Pheox}) and the protein. ATP was specifically incorporated in its binding site upon photosensitized irradiation. The amino acid could be linked to I on UV irradiation, either in the free state, engaged in the adenylate, or bound to the tRNA. The tRNA, ATP, and the amino acid linked to the tRNA interacted exclusively with the .beta. subunit (mol. wt. 63,000). The phenylalanine residue, either free or joined to the adenylate, could be crosslinked with equal efficiency to either type of subunit, suggesting that the amino acid binding site is located in a contact area between the 2 subunits. The Schiff base formation between tRNA^{Pheox} and I shows the existence of a lysyl group close to the binding site for the 3'-terminal adenosine of tRNA. This result was confirmed by the study of the inhibition of yeast I with pyridoxal phosphate and the 2',3'-dialdehyde derivative of ATP.

IT 54970-91-1

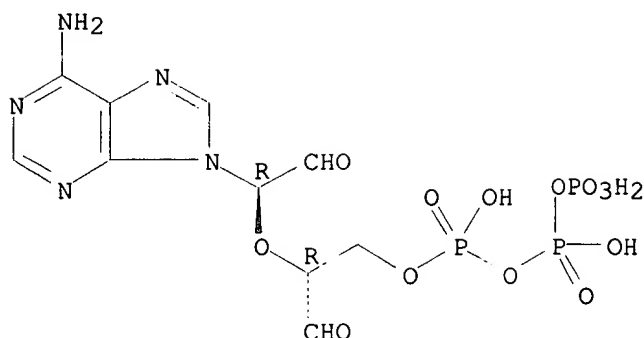
RL: BIOL (Biological study)

(phenylalanyl-transfer RNA synthetase inhibition by)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 206 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1979:201339 Document No. 90:201339 Factors influencing the response of human blood platelets to analogs of ADP which may act as partial agonists at the ADP receptor. Egan, Christopher M.; Fisher, Antony P.; Scrutton, Michael C. (Dep. Biochem., Univ. London, London, Engl.). Eur. J. Biochem., 95(1), 127-37 (English) 1979. CODEN: EJBCAI. ISSN: 0014-2956.

AB The prior addn. of nonaggregating concns. of the divalent cation ionophore A-23187 caused human platelets to aggregate in response to a subsequent addn. of the 2',3'-dialdehyde and 2',3'-dialc. derivs. of ADP (oADP and orADP, resp.), which act as partial agonists at the platelet ADP receptor inducing only the transition from discoid to globular morphol. (shape change). A secretion response was also obsd. on addn. of a low concn. of ionophore A-23187 prior to orADP. These responses were not obsd. if ionophore A-23187 was added prior to the 2',3'-dialdehyde and 2',3'-dialc. derivs. of ATP (oATP and orATP, resp) and were markedly inhibited by prior addn. of the ADP antagonist adenosine 5'-[.beta.,.gamma.-methylene]triphosphate. The aggregation response to oADP in the presence of ionophore A-23187 was reduced but not eliminated by addn. of 3 mM EGTA when studies were performed in heparinized platelet-rich plasma. Addns. of 3 mM EGTA in citrated platelet-rich plasma or 4 mM EDTA in either system completely inhibited this response. Inhibitors which were reported to elevate the intracellular concn. of cyclic AMP or to prevent Ca²⁺ movement also inhibited the aggregation response to oADP which was obsd. in the presence of ionophore A-23187. Prior addn. of inhibitors of adenylate cyclase failed to cause an aggregation response to subsequent addn. of oADP or orADP. Certain of these inhibitors enhanced and prolonged the shape change response to oADP or orADP but only at concns. an order of magnitude in excess of those required to antagonize inhibition by agents such as PGE₁, which act by increasing the concn. of cyclic AMP. The concn. of PGE₁, adenosine, or papaverine required to inhibit shape change induced by oADP was 1-2 orders of magnitude lower than that required to inhibit shape change induced by ADP. Prior addn. of oADP decreased the lag phase in the response of human platelets to arachidonate while also increasing the concn. required to observe half-maximal response and causing a decrease in the extent of that response. Prior addn. of oATP also diminished the extent of this response and increased the concn. of arachidonate required but had no effect on the lag phase. Evidently, oADP and orADP are capable only of acting as partial agonists at the ADP receptor because of a defective ability to increase cytosolic Ca²⁺ concn. This defect is rectified by the presence of low concns. of ionophore A-23187, which promotes mobilization of Ca²⁺ from an intracellular store. The results do not appear consistent with the thesis that a decrease in platelet cyclic AMP is an initiating event in aggregation induced by ADP, but do support a model which implicates cyclic AMP in depletion of cytosolic Ca²⁺.

IT 64060-84-0

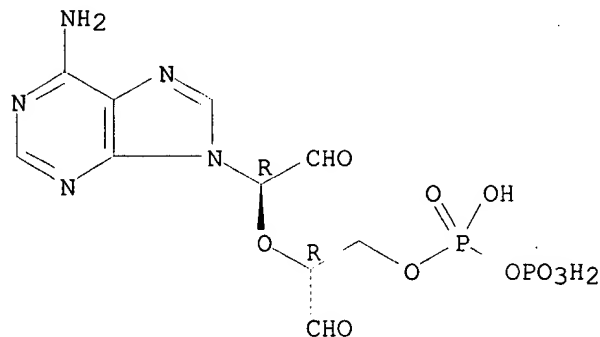
RL: BIOL (Biological study)

(blood platelet aggregation and shape change response to)

RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 58176-57-1

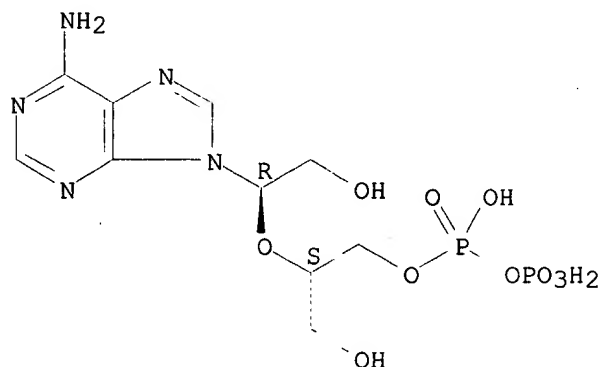
RL: BIOL (Biological study)

(blood platelet aggregation response to)

RN 58176-57-1 HCAPLUS

CN Diphosphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 207 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1979:199579 Document No. 90:199579 Affinity labeling of coupling

factor-latent ATPase from Mycobacterium phlei with 2',3'-dialdehyde derivatives of adenosine 5'-triphosphate and adenosine 5'-diphosphate.

Kumar, Gyanendra; Kalra, Vijay K.; Brodie, Arnold F. (Sch. Med., Univ. Southern California, Los Angeles, Calif., USA). J. Biol. Chem., 254(6), 1964-71 (English) 1979. CODEN: JBCHA3. ISSN: 0021-9258.

AB The 2',3'-dialdehyde deriv. of ATP (dial-ATP) was an affinity label for the ATP binding site of the latent ATPase from M. phlei. This analog of ATP caused the progressive inactivation of both the latent and unmasked ATPase with a K_i of 10 mM and min. inactivation half-times of 3 min and 21 min, resp. Stoichiometric studies of the inactivation process indicated that there was 1 ATP binding site/mol. purified ATPase. Latent and unmasked ATPase had an ATP binding site on .alpha. or .alpha.' subunit, resp. After inactivation by dial-ATP, latent ATPase was able to rebind to

Searched by: Mary Hale 308-4258 CM-1 12D16

membranes which were depleted of latent ATPase-coupling factor. The reconstituted membranes were capable of oxidative phosphorylation with exogenous ADP as the phosphate acceptor, indicating that different sites are involved in ATP hydrolysis and ATP synthesis. Affinity labeling of ADP binding sites with the 2',3'-dialdehyde deriv. of ADP revealed that the ADP binding site was present in both .alpha. and .beta. subunits of latent ATPase. The extent of the specific labeling in the .alpha. subunit was twice that obsd. in the .beta. subunit. Dial-ADP did not act as a phosphate acceptor in coupling of phosphorylation to oxidn. in *M. phlei* membrane preps. The results indicate that the .alpha. subunit of ATPase of *M. phlei* which binds ATP plays an important role in the hydrolysis of ATP.

IT 54970-91-1 64060-84-0

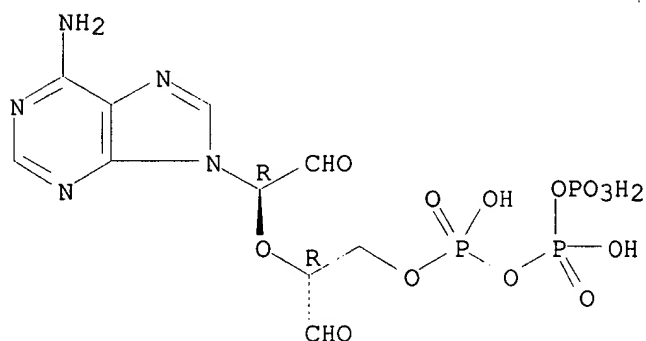
RL: BIOL (Biological study)

(ATPase of Mycobacterium affinity labeling with)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

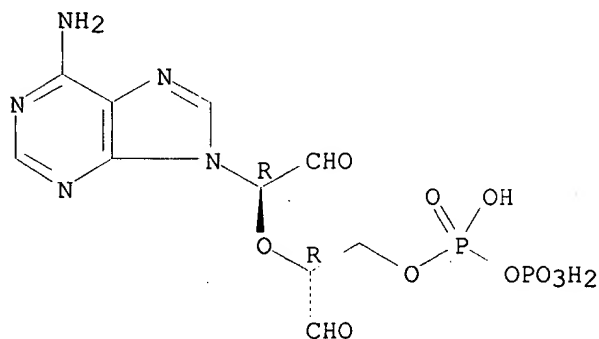
Absolute stereochemistry.



RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 208 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1979:35503 Document No. 90:35503 Activity of polynucleotide phosphorylase with nucleoside diphosphates containing sugar ring modifications. Hawley, D. M.; Sninsky, J. J.; Bennett, G. N.; Gilham, P. T. (Dep. Biol. Sci., Purdue Univ., West Lafayette, Indiana, USA). Biochemistry, 17(11), 2082-6 (English) 1978. CODEN: BICHAW. ISSN: 0006-2960.

Searched by: Mary Hale 308-4258 CM-1 12D16

AB A no. of nucleoside 5'-diphosphates contg. modifications in their sugar rings were synthesized, and the capacity of these nucleotides to act as substrates for polynucleotide phosphorylase was examd. The 5'-diphosphates of 9- β -D-arabinofuranosyladenine (ara-A) and 3'-deoxyadenosine were prepd. by phosphorylation of the nucleosides with POC13 followed by condensation of the resulting 5'-phosphates with inorg. phosphate using 1,1'-carbonyldiimidazole as the activating agent. The 5'-diphosphate of each ox-red nucleoside (a nucleoside in the the C2'-C3' bond has been cleaved) was synthesized by oxidn. of the 2',3'-cis-diol groups in the 5'-diphosphates of adenosine, cytidine, guanosine, and uridine with NaIO4 followed by the redn. of the resulting dialdehydes with NaBH4. Similar conditions were also used to prep. the ox-red nucleosides as well as their 5'-phosphates and 5'-triphosphates. In a study of the capacity of modified nucleotides to add to a small oligoribonucleotide in the presence of polynucleotide phosphorylase, 2 classes of activity were exhibited: (1) the addn. of a few residues of the nucleotide as in the case of the diphosphates of ara-A, 2'-deoxynucleosides, and (under certain conditions) 2'-O-(α -methoxyethyl)nucleosides; (2) the addn. of only 1 nucleotide residue as in the case of the diphosphates of the ox-red nucleosides and 3'-deoxyadenosine. The activity displayed by the latter class may be of value as a method for the radioactive labeling of the 3'-terminal ends of polyribonucleotides and RNA.

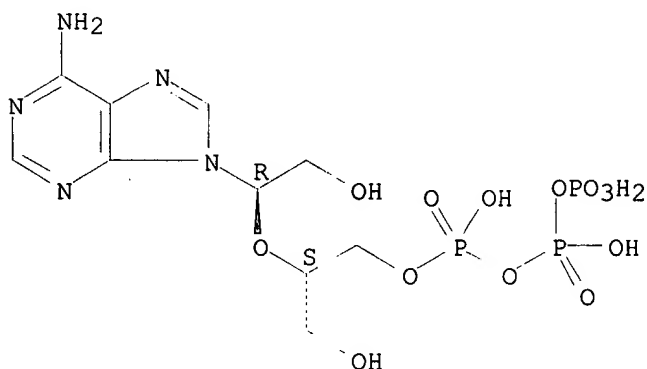
IT **35677-98-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 35677-98-6 HCAPLUS

CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



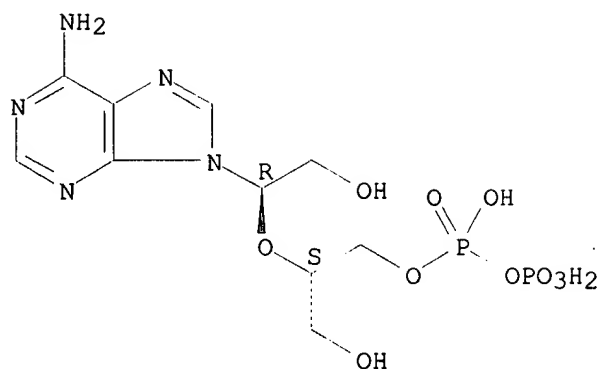
IT **58176-57-1**

RL: RCT (Reactant)
(reaction of, with polynucleotide phosphorylase and adenosine trinucleotide)

RN 58176-57-1 HCAPLUS

CN Diphosphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 209 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:560853 Document No. 89:160853 Interaction of human blood platelets with the 2',3'-dialdehyde and 2',3'-dialcohol derivatives of adenosine 5'-diphosphate and adenosine 5'-triphosphate. Pearce, P. Helen; Wright, Judith M.; Egan, Christopher M.; Scrutton, Michael C. (Dep. Biochem., Univ. London King's Coll., London, Engl.). Eur. J. Biochem., 88(2), 543-54 (English) 1978. CODEN: EJBICAI. ISSN: 0014-2956.

AB The 2',3'-dialdehyde deriv. of ADP (oADP) at concns. approaching the millimolar range induces human blood platelets to undergo shape change, but is incapable of inducing aggregation. When incubated with platelets for 1 min before addn. of the agonist, oADP acts as a competitive inhibitor of shape change and aggregation induced by ADP. Under these conditions secretion and hence aggregation induced by low concns. of collagen, and secretion and hence secondary aggregation induced by adrenaline, thrombin and vasopressin are also inhibited by this analog. In addn., oADP stimulates the rate of primary aggregation induced by adrenaline and causes partial inhibition of primary aggregation induced by thrombin or vasopressin. When longer preincubation times are employed the extent of inhibition with respect to all agonists, except for high concns. of collagen, is increased and the competitive character of the inhibition with respect to ADP is no longer apparent. Incubation of human platelets with the 2',3'-dialdehyde deriv. of ATP (oATP) causes effects similar to those for oADP except that the analog neither induces platelet shape change, nor stimulates the rate of primary aggregation induced by adrenaline. In addn. oATP fails to cause significant inhibition of platelet shape change induced by serotonin. The inhibition caused by oATP is not a function of the time of incubation. The 2',3'-dialc. derivs. of ADP and ATP (orADP and orATP) effect the aggregation properties of human blood platelets in a manner generally resembling those obsd. for the 2',3'-dialdehyde analogs. However, orADP is only weakly effective in causing platelet shape change and stimulating the rate of primary aggregation induced by adrenaline and does not inhibit secretion induced by adrenaline, collagen, thrombin, and vasopressin. The inhibition by orADP increases only slightly with increased time of incubation. Apparently, oADP acts as a partial agonist, whereas oATP and orADP as antagonists for the platelet ADP receptor.

IT 35677-98-6 54970-91-1 58176-57-1
64060-84-0

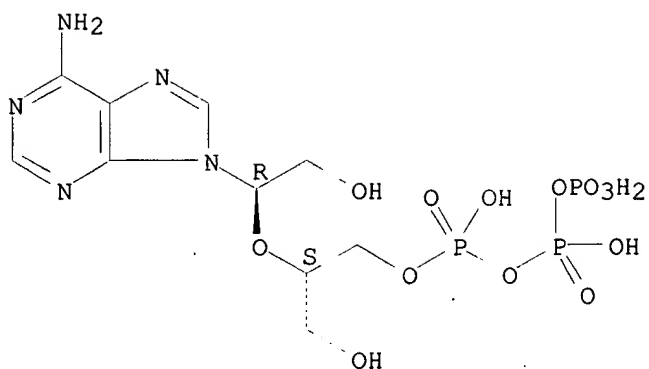
RL: BIOL (Biological study)
(blood platelet aggregation and morphol. response to)

RN 35677-98-6 HCAPLUS

CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

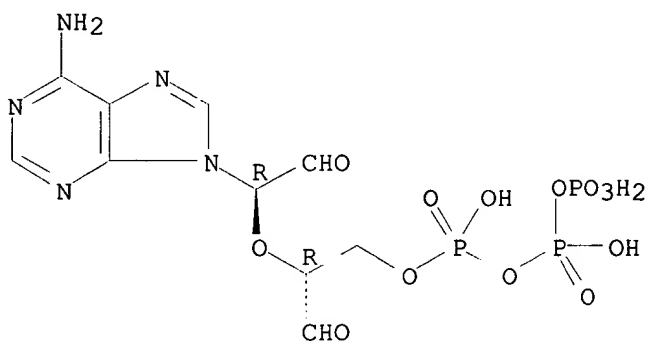
Searched by: Mary Hale 308-4258 CM-1 12D16



RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

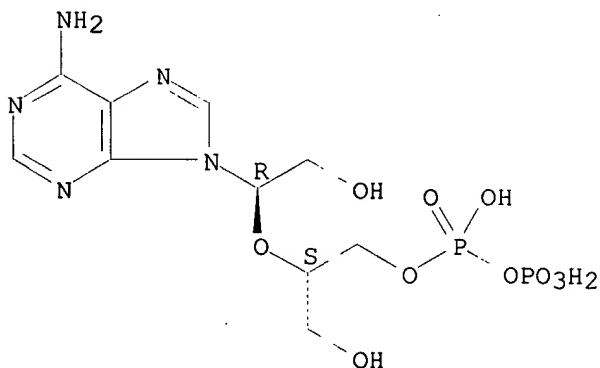
Absolute stereochemistry.



RN 58176-57-1 HCAPLUS

CN Diposphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

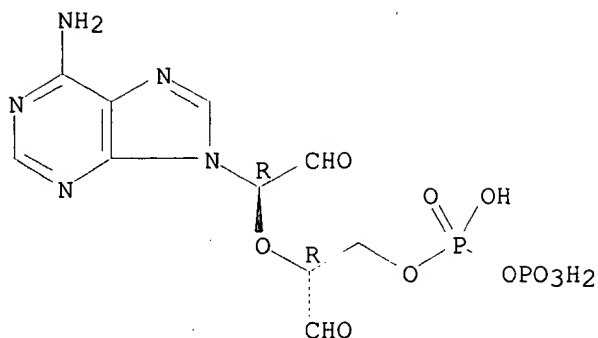


RN 64060-84-0 HCAPLUS

CN Diposphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



L14 ANSWER 210 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:525139 Document No. 89:125139 The requirements of cis-diol grouping and riboside structure in adenine-containing drugs for the inhibitory action on the activity of rat myocardial protein kinase. Hynie, Sixtus; Smrt, Jiri (Fac. Med., Charles Univ., Prague, Czech.). Collect. Czech. Chem. Commun., 43(6), 1531-7 (English) 1978. CODEN: CCCCAK. ISSN: 0366-547X.

AB The influence of OH group masking in adenosine and its nucleotides on the activity of rat myocardial protein kinase was studied by measuring the incorporation of ³²P from ATP-³²P into histones. Compared with the inhibitory effect of AMP, ADP, and ATP, the adenosine nucleotide 2',3'-O-ethoxymethylene derivs. inhibited incorporation only weakly. Acyclic 9-[1',5'-dihydroxy-4'(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]adenine 5'-diphosphate had no effect on kinase activity. The active site of protein kinase apparently requires both OH groups and a rigid configuration in the ribose moiety.

IT 58176-57-1

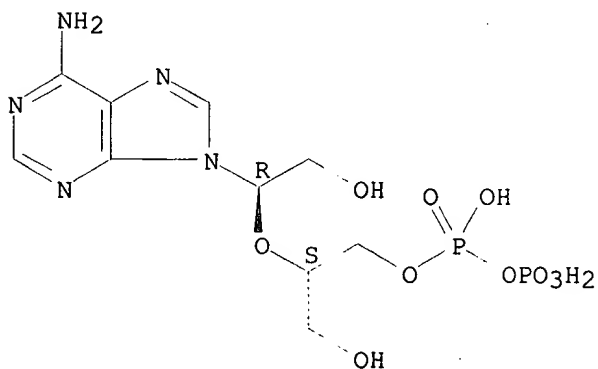
RL: BIOL (Biological study)

(protein kinase response to, structure in relation to)

RN 58176-57-1 HCAPLUS

CN Diphosphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 211 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:502612 Document No. 89:102612 Adenosine 5'-diphosphate dialdehyde: an affinity labeling reagent for phenol-sulfotransferase. Borchardt, Ronald T.; Wu, Su Er; Schasteen, Charles S. (Dep. Biochem., Univ. Kansas, Lawrence, Kans., USA). Biochem. Biophys. Res. Commun., 81(3), 841-9 (English) 1978. CODEN: BBRCA9. ISSN: 0006-291X.

Searched by: Mary Hale 308-4258 CM-1 12D16

AB 5'-ADP was oxidized with periodic acid to 2'-O-[(R)-formyl(adenin-9-yl)methyl]-3'-diphosphate-3'-deoxy-(s)-glyceraldehyde (ADP-dialdehyde). ADP-dialdehyde, but not 2',3'-acyclic ADP, inhibited phenol sulfotransferase (PST). The inhibition of PST by ADP-dialdehyde was irreversible. Kinetic anal. of the enzyme inactivation suggested the formation of a dissociable enzyme-inhibitor complex prior to the inactivation step. PST was completely protected from inactivation by the inclusion of 3'-phosphoadenosine-5'-phosphosulfate in the preincubation mixt. These results are consistent with ADP-dialdehyde being an affinity labeling reagent for PST.

IT **64060-84-0**

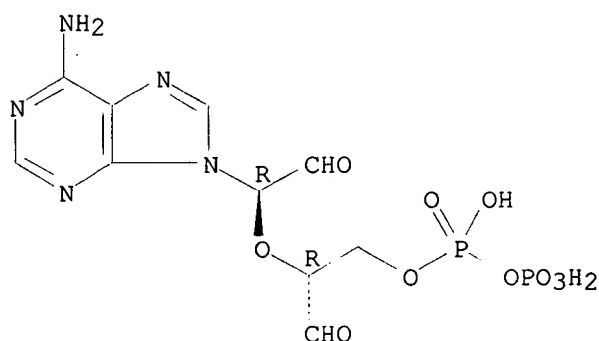
RL: BIOL (Biological study)

(phenol sulfotransferase inhibition and affinity labeling by)

RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

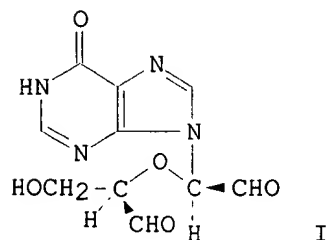
Absolute stereochemistry.



L14 ANSWER 212 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:499756 Document No. 89:99756 Inhibition of RNA synthesis in Ehrlich tumor cells by the dialdehyde derivative of inosine (NSC 118994). Cory, Joseph G.; Parker, Sandra H.; Fox, Cynthia S. (Dep. Biochem., Univ. South Florida Coll. Med., Tampa, Fla., USA). Cancer Res., 38(3), 815-22 (English) 1978. CODEN: CNREA8. ISSN: 0008-5472.

GI



AB NSC 118994 (inosine dialdehyde)(I) [23590-99-0] was studied for its effect on RNA synthesis in Ehrlich tumor cells. I inhibited the incorporation of [14C]uridine into the RNA of intact tumor cells. The synthesis of preribosomal RNA and high-mol.-wt. RNA was inhibited by I. ATP dialdehyde [54970-91-1] and inosine 5'-triphosphate

Searched by: Mary Hale 308-4258 CM-1 12D16

dialdehyde [66671-99-6] inhibited RNA synthesis in isolated nuclei. 5'-Inosinic acid dialdehyde [66672-00-2] and I when they were added to isolated nuclei did not inhibit RNA synthesis. However, when tumor cells were incubated with I or 5'-inosinic acid dialdehyde and the nuclei were then isolated, there was a marked decrease in RNA synthesis. This inhibition was both time and concn. dependent. The inhibition of RNA synthesis in the nuclei from treated cells was not reversed by changing the culture medium. .alpha.-Amanitin and actinomycin D inhibited RNA polymerase activities in the nuclei from control cells to the same extent that they inhibited the residual activity in the nuclei from the treated cells. Nuclear exts. prepd. from the I-treated cells did not show a decrease in RNA polymerase [9014-24-8] activity, indicating a reversal of the inhibition. The inhibition of RNA synthesis in the nuclei from I-treated cells was completely reversed by the addn. of exogenous poly(deoxyadenylate-deoxythymidylate) [26966-61-0] as template, showing that the inhibition of RNA synthesis by I was not due to the inhibition of RNA polymerases but rather was due to chain termination of the growing RNA strand or impairment of template function.

IT 54970-91-1

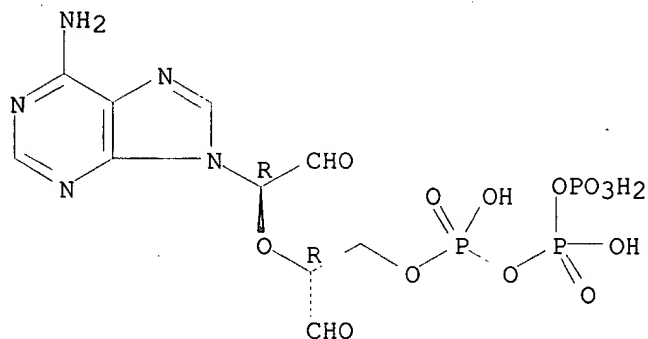
RL: BIOL (Biological study)

(RNA inhibition by, inosine dialdehyde in relation to)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 213 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:455559 Document No. 89:55559 Aminoacyl-tRNA synthetases: Affinity labeling of the ATP binding site by 2',3'-ribose oxidized ATP. Fayat, Guy; Fromant, Michel; Blanquet, Sylvain (Lab. Biochim., Ec. Polytech., Palaiseau, Fr.). Proc. Natl. Acad. Sci. U. S. A., 75(5), 2088-92 (English) 1978. CODEN: PNASA6. ISSN: 0027-8424.

AB Homogeneous Escherichia coli methionyl-, isoleucyl-, tryptophanyl-, and phenylalanyl-tRNA synthetases and Bacillus stearothermophilus methionyl- and tyrosyl-tRNA synthetases are irreversibly inactivated by reaction of their active ATP sites with the 2',3'-dialdehyde deriv. of ATP obtained by periodate oxidn. In each case, the amt. of 14C-labeled dialdehyde deriv. incorporated per mol. of inactivated enzyme appears consistent with the expected active stoichiometry of the synthetase. These results strongly support the presence, at the active site of the aminoacyl-tRNA synthetases, of a common residue, probably a lysine.

IT 54970-91-1

RL: BIOL (Biological study)

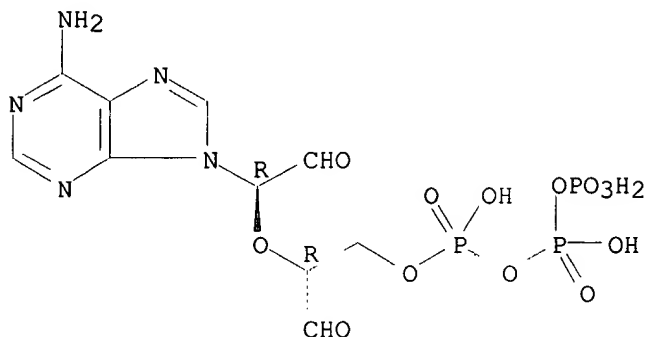
(aminoacyl-tRNA synthetase affinity labeling by)

RN 54970-91-1 HCAPLUS

Searched by: Mary Hale 308-4258 CM-1 12D16

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 214 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:439574 Document No. 89:39574 Studies on the tight adenine nucleotide binding site of chloroplast coupling factor (CF1). Strotmann, H.; Bickel-Sandkoetter, S.; Edelman, K.; Schlimme, E.; Boos, K. S.; Luestorff, J. (Bot. Inst., Tieraerztl. Hochsch. Hannover, Hannover, Ger.). BBA Libr., 14(Struct. Funct. Energy-Transducing Membr.), 307-17 (English) 1977. CODEN: BBALAJ. ISSN: 0067-2734.

AB A study of the specificities of 14 different ADP analogs in light-induced incorporation into membrane-bound chloroplast coupling factor (CF1), using 3-times-washed broken chloroplasts of spinach, indicated that the structural features of the ADP mol. required in the process of ATP formation are entirely different from those which are relevant in tight binding by CF1. In tight binding there was a high specificity for the adenine base, suggesting that the base moiety is the recognition site of the nucleotide mol. In the process of photophosphorylation, base specificity is different from that obtained in binding to CF1. Replacement of the amino group at C-6 by O (IDP, GDP) had a comparatively small effect on phosphorylation. In contrast, altering the N-1 of the heterocyclic ring (ADP-1-oxide, 1-amino- IDP) decreased the specificity to a much greater extent. In tight binding as well as in phosphorylation, anti-conformation of the adenine base relative to the sugar moiety appears to be required.

IT 58176-57-1

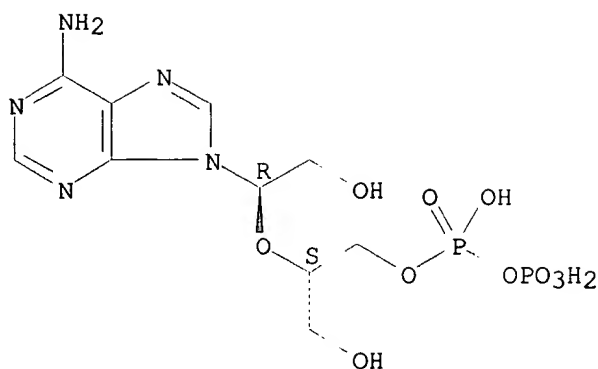
RL: BIOL (Biological study)

(light-induced binding of, by broken chloroplasts)

RN 58176-57-1 HCAPLUS

CN Diphosphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 215 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:438633 Document No. 89:38633 Substrate specificity of soluble mitochondrial ATPase. Kozlov, I. A.; Metel'skaya, V. A.; Mikhailov, S. N.; Novikova, I. Yu.; Florent'ev, V. L. (Dep. Bioenerg., A. N. Belozerskii Lab. Bioorg. Chem. Mol. Biol., Moscow, USSR). Biokhimiya (Moscow), 43(4), 702-7 (Russian) 1978. CODEN: BIOHAO. ISSN: 0006-307X.

AB The parameters of the hydrolysis of ATP and several analogs by sol. mitochondrial ATPase (I) were detd. The Vmax of the reaction decreased as follows: 2'-deoxy-ATP > ATP > etheno-ATP > GTP > 3'-O-methyl-ATP > UTP. ATP, 2'-deoxy-ATP, 3'-O-methyl-ATP, GTP, and etheno-ATP were hydrolyzed by I with similar apparent Km values. CTP was not hydrolyzed by I and did not inhibit the I reaction at a concn. of 10-2M. Nucleoside triphosphate derivs. with an open ribose ring, 9-[1',5'-dihydroxy-4'-(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]adenine-5'-triphosphate and 1-[1',5'-dihydroxy-4'-(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]cytosine-5'-triphosphate, were effective inhibitors of ATPase (Ki .apprx.5 .times. 10-5 M). I bound ATP analogs having hydrocarbon radicals, (CH2)2, (CH2)3, and (CH2)4, instead of the ribose residues. 9-(3'-Hydroxypropyl)-adenine-3'-triphosphate and 9-(4-hydroxybutyl)adenine-4'-triphosphate were not hydrolyzed by I, although they inhibited the I reaction (Ki = 2 .times. 10-4 M). 9-(2'-Hydroxyethyl)adenine-2'-triphosphate was hydrolyzed by I 8-fold more slowly than ATP. It is suggested that the hydrolysis of substrates of I is preceded by the binding of the substrates in a strained conformation in the active site.

IT 35677-98-6 55881-01-1 55881-02-2

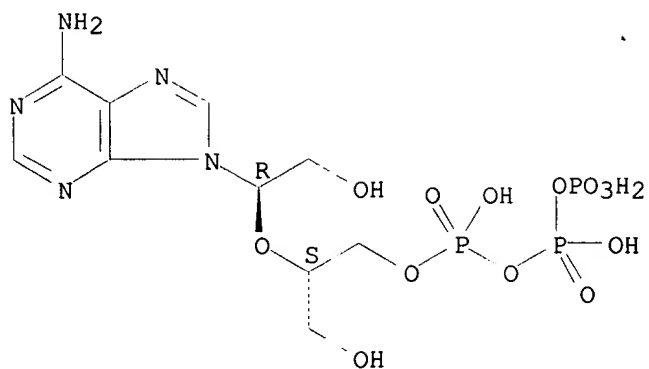
RL: BIOL (Biological study)

(ATPase inhibition by)

RN 35677-98-6 HCAPLUS

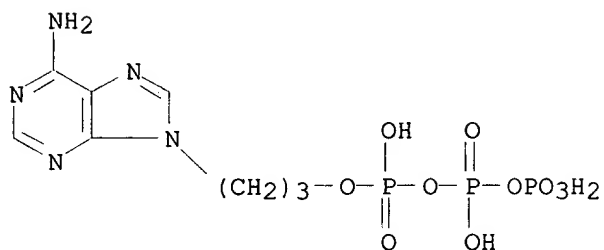
CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



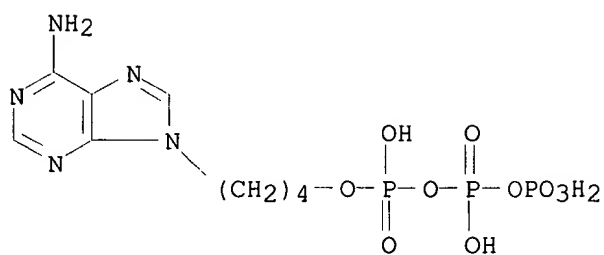
RN 55881-01-1 HCAPLUS

CN Triphosphoric acid, P-[3-(6-amino-9H-purin-9-yl)propyl] ester (9CI) (CA INDEX NAME)



RN 55881-02-2 HCAPLUS

CN Triphosphoric acid, P-[4-(6-amino-9H-purin-9-yl)butyl] ester (9CI) (CA INDEX NAME)

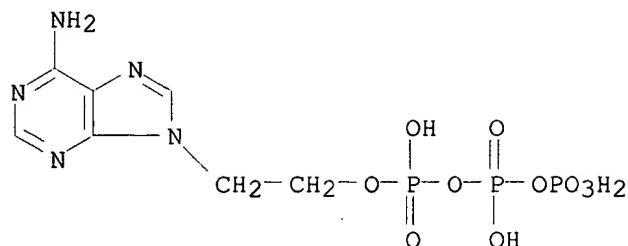


IT 55881-00-0

RL: RCT (Reactant)
(reaction of, with ATPase)

RN 55881-00-0 HCAPLUS

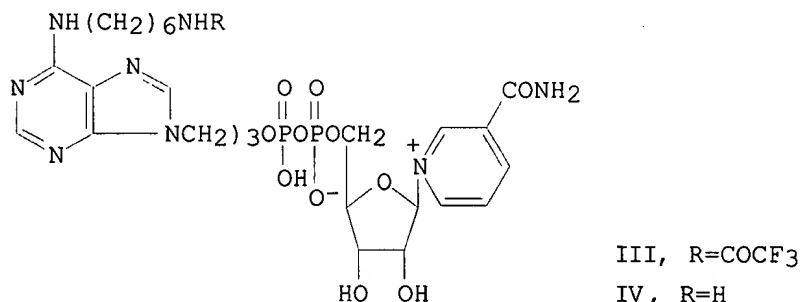
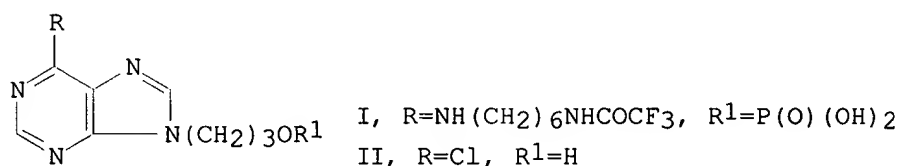
CN Triphosphoric acid, P-[2-(6-amino-9H-purin-9-yl)ethyl] ester (9CI) (CA INDEX NAME)



L14 ANSWER 216 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:185183 Document No. 88:185183 The coenzyme analog (3-[6-(6-aminohexylamino)-9-puriny]propyl)(nicotinamide-D-ribose)diphosphate as ligand for affinity chromatography of dehydrogenases. Berariu, Veronica; Jeck, Reinhard; Woenckhaus, Christoph (Gustav-Embden-Zent. Biol. Chem., Univ. Frankfurt, Frankfurt/Main, Ger.). Justus Liebigs Ann. Chem. (1), 118-23 (German) 1978. CODEN: JLACBF. ISSN: 0075-4617.

GI



AB 9-[3-(Dihydroxyphosphoryloxy)propyl]-6-[6-(trifluoroacetylaminohexylamino)-9H-purine (I) was prepd. starting from 6-chloro-9-(3-hydroxypropyl)-9H-purine (II). After condensation of this AMP-analog with dicyclohexylcarbodiimide and NMN in aq. pyridine, a new NAD-analog was formed. The coenzyme analog (3-[6-(6-trifluoroacetylaminohexylamino)-9-puriny]propyl)(nicotinamide-D-ribose)diphosphate (III) acted as H acceptor (its reduced form as H donor) when tested against different dehydrogenases. Highly dissocd. complexes between this coenzyme analog and dehydrogenases were formed. Removal of the trifluoroacetyl group led to the unstable coenzyme analog (3-[6-(6-aminohexylamino)-9-puriny]propyl)(nicotinamide-D-ribose)diphosphate (IV), which can be covalently attached to agarose activated with CNBr. When dehydrogenases were applied to the column of the immobilized AMP and NAD-analogs, only glyceraldehyde 3-phosphate dehydrogenase was retained. Elution of the enzyme occurred only after addn. of KCl to the eluant.

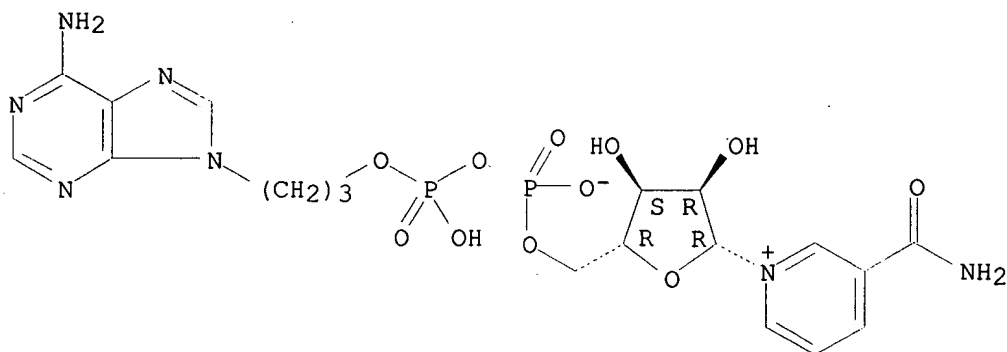
IT 42188-23-8

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(as dehydrogenase coenzyme)

RN 42188-23-8 HCAPLUS

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[7-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahept-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 66443-32-1P

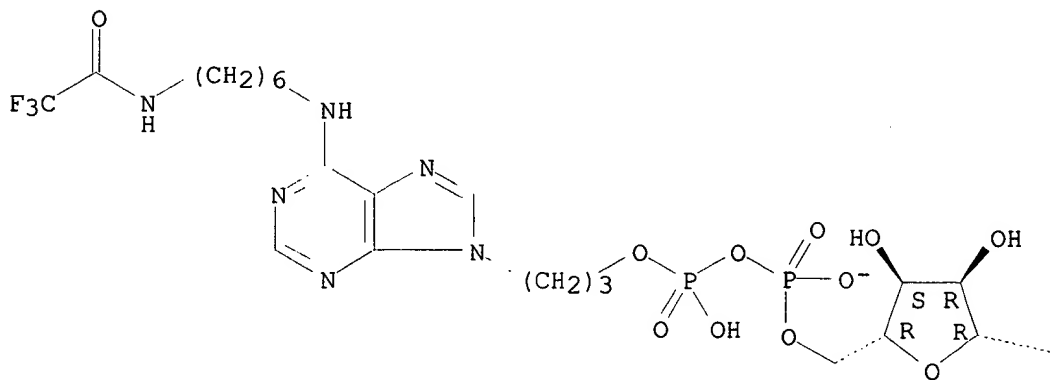
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and coenzyme properties of)

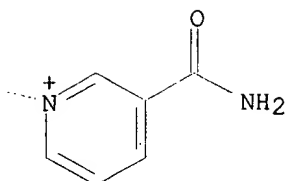
RN 66443-32-1 HCAPLUS

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[hydroxy[[hydroxy[3-[6-[[6-[(trifluoroacetyl)amino]hexyl]amino]-9H-purin-9-yl]propoxy]phosphinyl]oxy]phosphinyl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





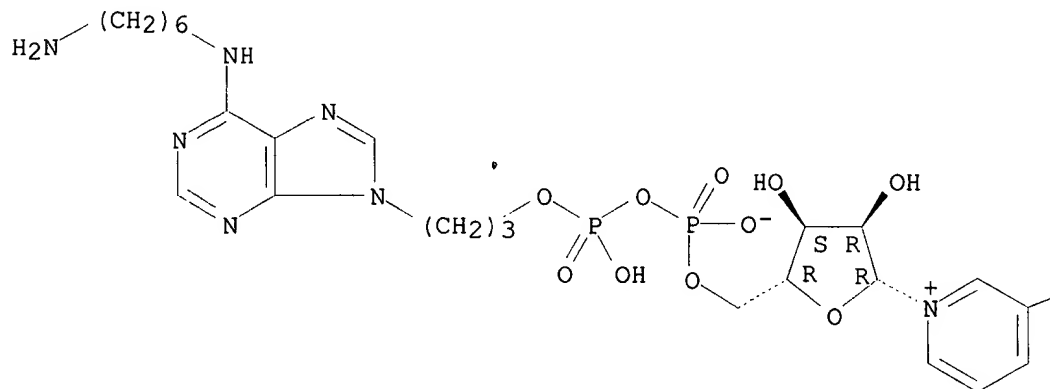
IT 66443-33-2P

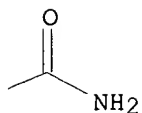
RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(prepn. of and dehydrogenase affinity chromatog. in relation to)

RN 66443-33-2 HCAPLUS

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[7-[9-[(6-aminohexyl)amino]-9H-purin-9-yl]-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahept-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.





L14 ANSWER 217 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:100848 Document No. 88:100848 Characterization of ligand affinities for (sodium, potassium)-activated ATPase. Henke, W.; Schoen, R. (Zentralinst. Molekularbiol., DAW, Berlin-Buch, E. Ger.). *Ergeb. Exp. Med.*, 24(Biol. Regul. Intermol. Wechselwirkungen), 189-94 (German) 1977. CODEN: EREMAH. ISSN: 0374-7506.

AB Na⁺,K⁺-ATPase showed no enzyme activity with ATP-dialdehyde (I) in the place of ATP; however, the kinetics of ouabain binding were similar in both systems. No acid-stable phosphorylated intermediate was formed with I, thus permitting the Mg²⁺ affinity and the influence of Mg²⁺ on the binding of other cations by ATPase to be detd. At low Mg²⁺ concns. in the presence of I, the Na⁺ affinity was very low compared to the active ATPase system; at higher Mg²⁺ concns., the K_{0.5} for Na⁺ increased. Na⁺ activated ouabain binding at low concns. and inhibited at high concns. Increasing Na⁺ concns. decreased K⁺ affinity for enzyme. In the system contg. I, the Mg²⁺ affinity was 0.88 .mu.M in the presence of 3 mM Na⁺ and 8.4 .mu.M in the presence of 80 mM Na⁺. The effect of ATP concn. on ouabain binding was also characterized. The results are discussed with ref. to the flip-flop model of ATPase function.

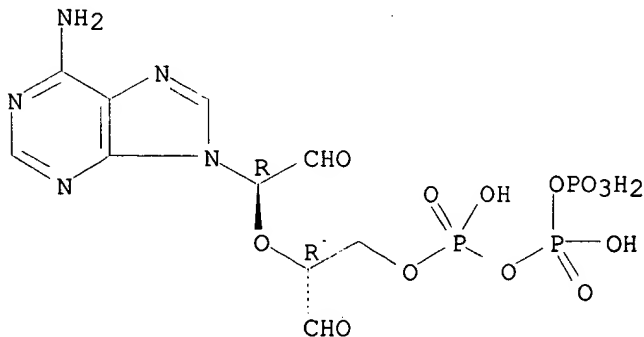
IT 54970-91-1

RL: PROC (Process)
(ATPase binding of)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 218 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1978:46897 Document No. 88:46897 Enzymic incorporation of ATP and CTP

Searched by: Mary Hale 308-4258 CM-1 12D16

analogues into the 3' end of tRNA. Sprinzl, Mathias; Sternbach, Hans; Von der Haar, Friedrich; Cramer, Friedrich (Abt. Chem., Max-Planck-Inst. Exp. Med., Goettingen, Ger.). Eur. J. Biochem., 81(3), 579-89 (English) 1977. CODEN: EJBCAI.

- AB Structural analogs of ATP and CTP were investigated as substrates for ATP(CTP):tRNA nucleotidyltransferase (I). Eight out of 26 ATP analogs and 6 out of 9 CTP analogs were incorporated into the 3' terminus of tRNA. In general, for the recognition of the substrates the modification of the cytidine is less crit. than is the modification of adenosine. An isosteric substitution on the ribose residue is possible in both CTP and ATP. The free hydroxyls of these triphosphates can be replaced by an NH₂ group or H without loss of substrate properties. Modifications of positions 1, 2, 6, and 8 on the adenine ring of ATP are not allowed whereas modification on positions 2, 4, and 5 on the cytosine ring of CTP are tolerated by I. No differences can be obsd. in the substrate properties of I of different sources. Methods of prepn. of tRNA species, which are shortened at their 3' end by .gtoreq.1 nucleotide, and anal. procedures for characterization of these modified tRNAs are described.

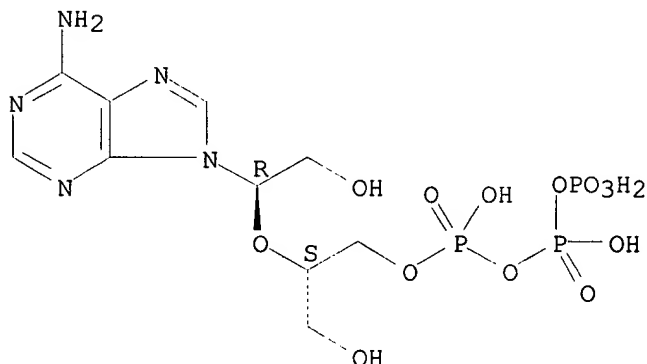
IT 35677-98-6

RL: BIOL (Biological study)
(as tRNA nucleotidyltransferase substrate)

RN 35677-98-6 HCAPLUS

CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 219 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1977:546446 Document No. 87:146446 Interaction of human blood platelets with the 2',3'-dialdehyde derivatives of adenosine diphosphate and adenosine triphosphate. Pearce, P. Helen; Scrutton, Michael C. (Dep. Biochem., King's Coll., London, Engl.). Biochem. Soc. Trans., 5(1), 138-9 (English) 1977. CODEN: BCSTB5.

- AB Incubation of human blood platelets with ADP 2',3'-dialdehyde deriv. (I) [64060-84-0] (1.6mM) caused a substantial shape-change but did not induce aggregation; 1.6mM I inhibited, apparently competitively, the shape-change and aggregation induced by 5.mu.M ADP [58-64-0] by .apprx.70%. I was an effective inhibitor of collagen-induced aggregation; 3mM I only slightly decreased total aggregation induced by 5.mu.M adrenaline but there was a marked decrease in the rate of the secretory phase of the response. High concns. of I partially inhibited thrombin-induced aggregation. Incubation of human platelets with ATP 2',3'-dialdehyde deriv. (II) [54970-91-1] (.ltoreq.5mM) did not induce shape-change or aggregation of the platelets; the inhibitory effects of II on ADP-induced shape-change and aggregation and on adrenaline-induced aggregation were qual. similar to those obsd. for I.

Searched by: Mary Hale 308-4258 CM-1 12D16

Thus I and II may be suitable reagents for studies designed to isolate the ADP receptor of human platelets.

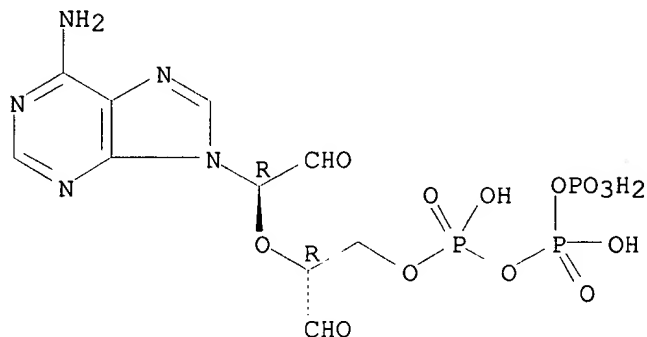
IT 54970-91-1 64060-84-0

RL: PRP (Properties)
(blood platelet interaction with)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

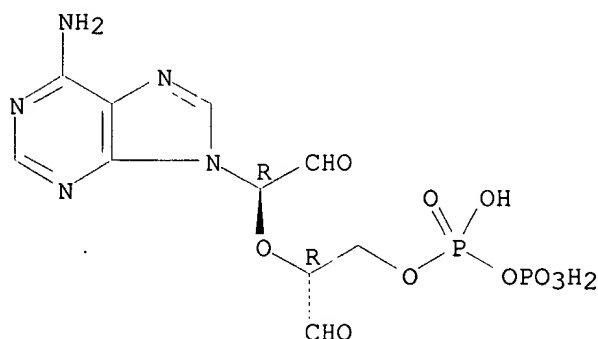
Absolute stereochemistry.



RN 64060-84-0 HCAPLUS

CN Diphosphoric acid, mono[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 220 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1977:529440 Document No. 87:129440 ATP analogs in the RNA-polymerase reaction. Aivazashvili, V. A.; Bibilashvili, R. Sh.; Florent'ev, V. L. (Inst. Mol. Biol., Moscow, USSR). Mol. Biol. (Moscow), 11(4), 854-63 (Russian) 1977. CODEN: MOBIBO.

AB Various nonglycosidic analogs of ATP were weak inhibitors of transcription in vitro, competing with ATP for the RNA polymerase binding site. Only 3'-O-methyl-ATP (but not 2'-O-methyl-ATP) was an effective inhibitor, causing irreversible inhibition of RNA synthesis at ionic strength 0.13 and 25.degree.. This was apparently due to its incorporation into the terminal position of the growing RNA chain. However, at increased temp. and ionic strength, 3'-O-methyl-ATP became a reversible competitive inhibitor with a K_i of 4 .times. 10⁻⁵M. The mechanism of inhibition was discussed.

IT 35677-98-6 55881-00-0 55881-01-1
55881-02-2

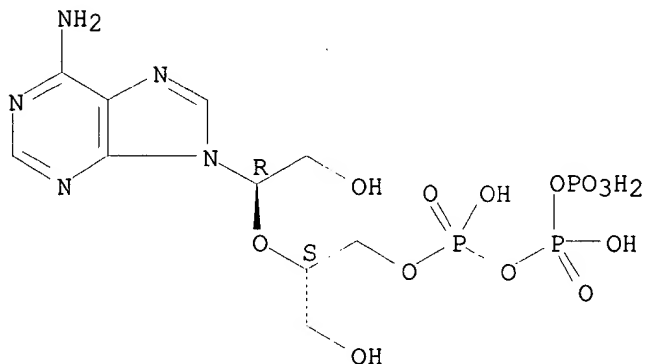
Searched by: Mary Hale 308-4258 CM-1 12D16

RL: BIOL (Biological study)
(RNA polymerase inhibition by)

RN 35677-98-6 HCAPLUS

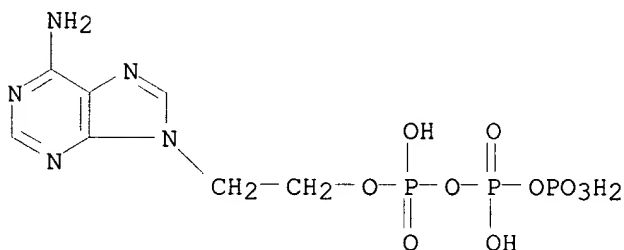
CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



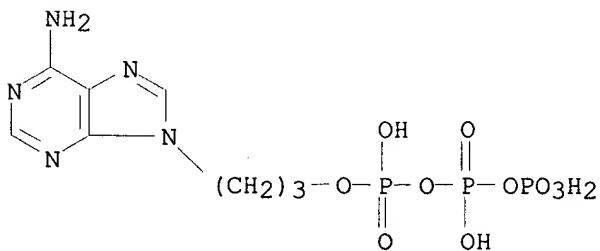
RN 55881-00-0 HCAPLUS

CN Triphosphoric acid, P-[2-(6-amino-9H-purin-9-yl)ethyl] ester (9CI) (CA INDEX NAME)



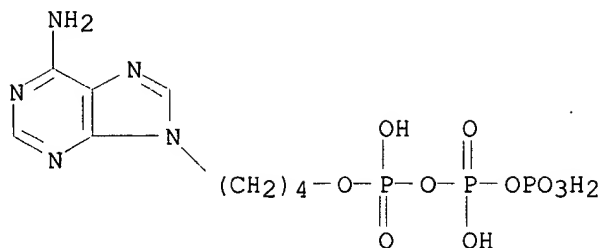
RN 55881-01-1 HCAPLUS

CN Triphosphoric acid, P-[3-(6-amino-9H-purin-9-yl)propyl] ester (9CI) (CA INDEX NAME)



RN 55881-02-2 HCAPLUS

CN Triphosphoric acid, P-[4-(6-amino-9H-purin-9-yl)butyl] ester (9CI) (CA INDEX NAME)



L14 ANSWER 221 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1977:434682 Document No. 87:34682 Interaction of adipic acid dihydrazide analog of ATP with myosin. Involvement of the essential sulfhydryl groups. Reisler, Emil; Lamed, Raphael (Polym. Dep., Weizmann Inst. Sci., Rehovot, Israel). Biochemistry, 16(11), 2532-8 (English) 1977. CODEN: BICHAW.

AB The hydrolysis by myosin of a sol. ATP analog, adipic acid dihydrazide-ATP (I), proceeds in a fashion similar to the hydrolysis of ATP by myosin modified at either of the 2 essential SH groups. In both systems, the Mg^{2+} -activated hydrolysis of the nucleotide is increased, whereas the EDTA-stimulated activity is inhibited. Blocking of SH1 or SH2 leads to a complete inhibition of I hydrolysis. I is unable to expose the SH2 for modification by thiol reagents. Apparently, I need interact with only 1 of the 2 essential thiol sites of myosin. The hydrolysis of Mg-I by myosin is inhibited by a large excess of actin and does not result in contraction of actomyosin threads. Mg-I is also a rather weak dissociation agent of the acto-heavy meromyosin complex. These properties of I are discussed in conjunction with modification studies of myosin and the mechanism of ATP hydrolysis.

IT 63713-53-1

RL: RCT (Reactant)

(myosin ATPase hydrolysis of, mercapto groups in relation to)

RN 63713-53-1 HCAPLUS

CN Hexanedioic acid, dihydrazide, polymer with $[R-(R^*, R^*)]-P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl]$ triphosphate (9CI) (CA INDEX NAME)

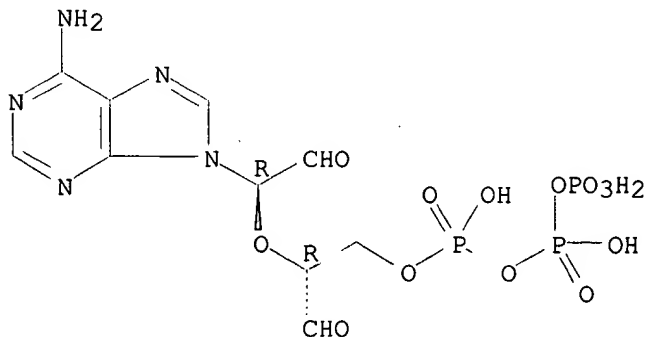
CM 1

CRN 54970-91-1

CMF C10 H14 N5 O13 P3

CDES 1:R2:R*, R*

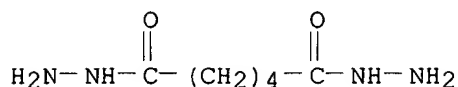
Absolute stereochemistry.



CM 2

CRN 1071-93-8

CMF C6 H14 N4 O2



L14 ANSWER 222 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1977:27753 Document No. 86:27753 Properties of ribose modified ADP analogs in photophosphorylation of spinach chloroplasts. Boos, Karl S.; Luestorff, Joachim; Schlimme, Eckhard (Inst. Klin. Biochem. Physiol. Chem., Med. Hochsch. Hannover, Hannover, Ger.). FEBS Lett., 71(1), 124-9 (English) 1976. CODEN: FEBLAL.

AB The nucleotide analogs 1,3'-dADP and 2'-dADP were able to serve as phosphoryl acceptors, whereas rroADP (2,2'[1-(9-adenyl)-1'-diphosphoryloxymethyl]dihydroxydiethyl ether) was not phosphorylated by spinach chloroplasts. However, all the adenine nucleotide analogs, including rroADP, were capable of binding to the same active site of CF1 of spinach chloroplast as the natural substrate ADP. Although it bound to CF1, rroADP was unable to form a stabilized Mg2+ complex involving the .alpha.- and .beta.-phosphate group and N(7) of the heterocyclic base.

IT 61504-13-0

RL: BIOL (Biological study)

(in photophosphorylation, by spinach chloroplasts)

RN 61504-13-0 HCAPLUS

L14 ANSWER 223 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1976:105964 Document No. 84:105964 Oligonucleotidic compounds. LVII. Free-conformational analogs of nucleotides and oligonucleotides derived from 9-[1',5'-dihydroxy-4'(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]adenine. Smrt, J.; Mikhailov, S. N.; Hynie, S.; Florent'ev, V. L. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, Czech.). Collect. Czech. Chem. Commun., 40(11), 3399-403 (English) 1975. CODEN: CCCCAK.

GI For diagram(s), see printed CA Issue.

AB AMP was transformed by NaIO4 oxidn. and NaBH4 redn. into 9-[1',5'-dihydroxy-4'(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]adenine 5'-phosphate (I). ADP, adenylyl-(3'.fwdarw.5')-adenosine, and uridylyl-(3'.fwdarw.5')-adenylyl-(3'.fwdarw.5')-adenosine were transformed analogously. With N,N'-dicyclohexylcarbodiimide, I gave 9-[1',5'-dihydroxy-4'-(1''-hydroxymethyl)-3'-oxapent-2'(R)-yl]adenine 5',1''-cyclic phosphate. 9-[1',5'-Dihydroxy-4'(S)-hydroxymethyl-3'-oxapent-2'(R)-yl]adenine 5'-diphosphate inhibited the polymn. of ADP with polynucleotide phosphorylase.

IT 58176-57-1P

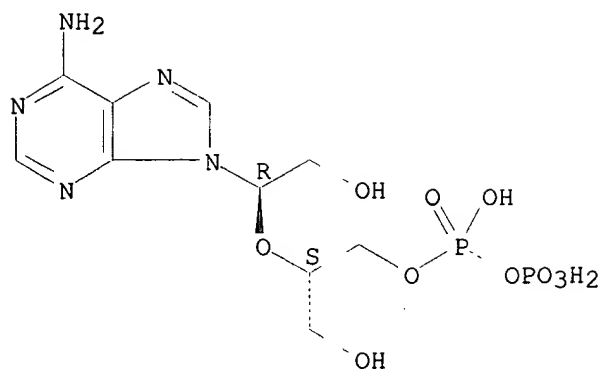
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and interaction with polynucleotide phosphorylase)

RN 58176-57-1 HCAPLUS

CN Diphosphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 224 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1976:101520 Document No. 84:101520 Pyruvate carboxylase: affinity labeling of the magnesium adenosine triphosphate binding site. Easterbrook-Smith, Simon B.; Wallace, John C.; Keech, D. Bruce (Dep. Biochem., Univ. Adelaide, Adelaide, Aust.). Eur. J. Biochem., 62(1), 125-30 (English) 1976. CODEN: EJBCAI.

AB The 2',3'-dialdehyde deriv. of ATP (oATP) was prepd. by periodate oxidn. and because of the following criteria was considered to be an effective affinity label. The Mg^{2+} complex of this deriv. (Mg -oATP $^{2-}$) was a linear competitive inhibitor with respect to Mg ATP $^{2-}$ in both the acetyl-CoA-dependent and -independent activities of the enzyme but was a noncompetitive inhibitor with respect to HCO_3^- , and an uncompetitive inhibitor with respect to pyruvate. Mg -oATP was covalently bound to pyruvate carboxylase by redn. using $NaBH_4$ with concurrent irreversible inactivation of the enzyme. Although HCO_3^- , pyruvate, and oxalacetate were ineffective, both Mg ATP $^{2-}$ and acetyl-CoA protected the enzyme against this chem. modification. At 100% inactivation, 1.1 ± 0.1 mole of Mg -oATP $^{2-}$ were bound to the enzyme/mole of biotin. Acetyl-CoA had no effect on this stoichiometry. Chromatog. of samples of an enzymic digest of Mg -o[^{14}C]ATP $^{2-}$ -labeled enzyme revealed 1 major band of radioactivity which cochromatog. with authentic Lys-oATP.

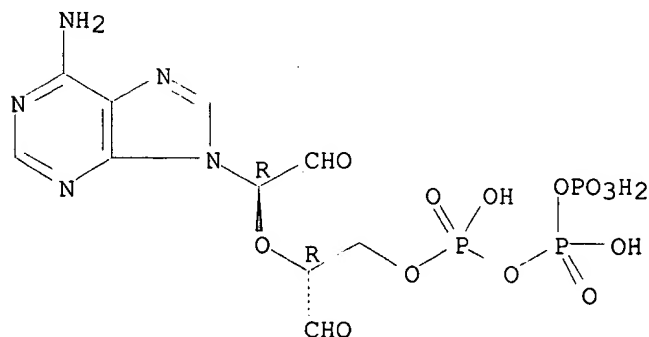
IT 54970-91-1

RL: BIOL (Biological study)
(pyruvate carboxylase affinity labeling by)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 225 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1976:55397 Document No. 84:55397 Properties of the ribose-ring-opened adenine nucleotide 2,2'-[1-(9-adenyl)-1'-(tri-, diphosphoryloxymethyl)]dihydroxydiethyl ether in mitochondrial adenine nucleotide translocation. Boos, Karl S.; Schlimme, Eckhard; Bojanovski, Dubo; Lamprecht, Walther (Inst. Klin. Biochem. Physiol. Chem., Med. Hochsch. Hannover, Hannover, Ger.). Eur. J. Biochem., 60(2), 451-8 (English) 1975. CODEN: EJBCAI.

AB 14C- or 32P-labeled 2,2'-[1-(9-adenyl)-1'-(tri-, diphosphoryloxymethyl)]dihydroxydiethyl ether (rroANP) was obtained from ANP by cleavage of the C-2'-C-3' bond by Na periodate oxidn. and subsequent borohydride redn. Binding of rroANP to rat liver mitochondria revealed carrier-linked atractyloside-sensitive and nonspecific atractyloside-insensitive binding but no transfer across the inner mitochondrial membrane. Kinetic data indicated rroANP as a competitive inhibitor for ANP uptake with $K_i = 9.3 \times 10^{-5}$ M. Exptl. rroANP confirmed that an intact adenine base and 3 anionic charges of the phosphate chain are essential for the recognition between ANP-carrier and nucleotide but unsufficient for the induction of a transmembrane ANP exchange. In addn., mobilization of the carrier-nucleotide complex required an intact ribofuranoside ring system.

IT 58176-57-1

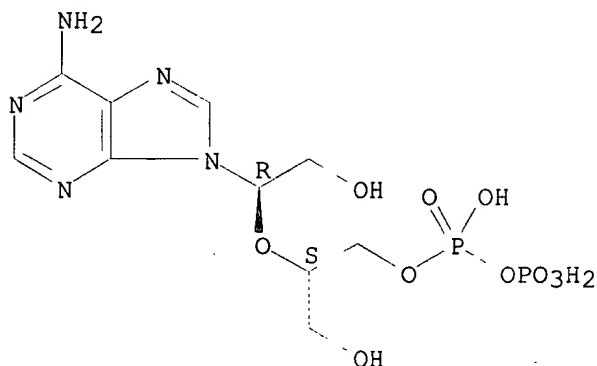
RL: BIOL (Biological study)

(adenine nucleotide transport by liver mitochondria inhibition by)

RN 58176-57-1 HCAPLUS

CN Diphosphoric acid, mono[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 35677-98-6

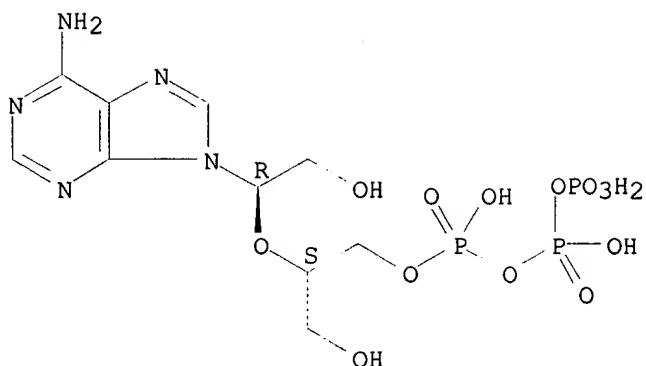
RL: BIOL (Biological study)

(adenine nucleotide transport by mitochondria inhibition by)

RN 35677-98-6 HCAPLUS

CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 226 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1976:4908 Document No. 84:4908 Nonglycoside analogs of nucleotides. 6. Mono- and triphosphates of .omega.-hydroxyalkyl derivatives of nucleic bases. Kritsyn, A. M.; Mikhailov, S. M.; Kolobushkina, L. I.; Padyukova, N. Sh.; Florent'ev, V. L. (Inst. Mol. Biol., Moscow, USSR). Izv. Akad. Nauk SSSR, Ser. Khim. (8), 1846-50 (Russian) 1975. CODEN: IASKA6.

GI For diagram(s), see printed CA Issue.

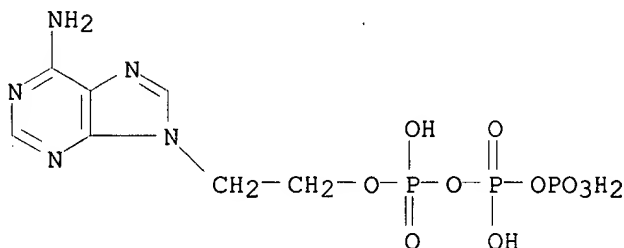
AB Monophosphates I, II, III [R = P(O)(OH)₂, n = 2, 3, 4] were obtained in 48-94% yields by phosphorylation of the corresponding alc. with cyanoethyl phosphate in the presence of N,N'-dicyclohexylcarbodiimide. Triphosphates I [R = P(O)(OH)OP(O)(OH)OP(O)(OH)₂, n = 4] and III [R = P(O)(OH)OP(O)(OH)OP(O)(OH)₂, n = 2, 3, 4] were obtained in 59-68% yields by phosphorylation of salts of the monophosphates with bis(tert-butylammonium) pyrophosphate.

IT 55881-00-0P 55881-01-1P 55881-02-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

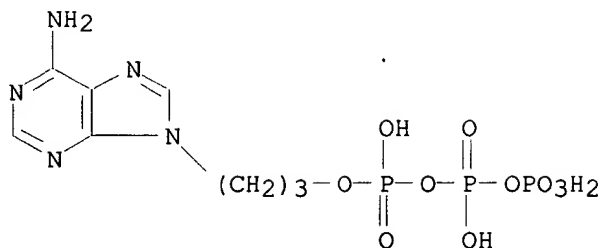
RN 55881-00-0 HCAPLUS

CN Triphosphoric acid, P-[2-(6-amino-9H-purin-9-yl)ethyl] ester (9CI) (CA INDEX NAME)



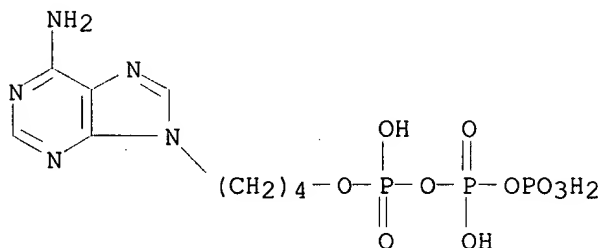
RN 55881-01-1 HCAPLUS

CN Triphosphoric acid, P-[3-(6-amino-9H-purin-9-yl)propyl] ester (9CI) (CA INDEX NAME)



RN 55881-02-2 HCAPLUS

CN Triphosphoric acid, P-[4-(6-amino-9H-purin-9-yl)butyl] ester (9CI) (CA INDEX NAME)



L14 ANSWER 227 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1975:493004 Document No. 83:93004 Stereochemical course of the adenosine triphosphate phosphoribosyltransferase reaction in histidine biosynthesis. Chelsky, Daniel; Parsons, Stanley M. (Dep. Chem., Univ. California, Santa Barbara, Calif., USA). J. Biol. Chem., 250(14), 5669-73 (English) 1975. CODEN: JBCHA3.

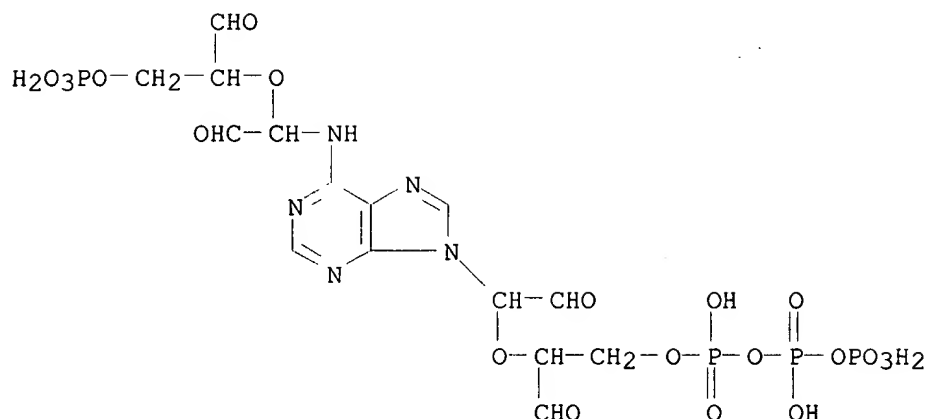
AB The product of the 1st reaction in histidine biosynthesis was shown by optical rotation measurements on 3 derivs. to have inverted, .beta. stereochem. at the newly formed bond. This is in contrast to .alpha. linkage expected on the basis of previously obsd. exchange, specificity, and covalent intermediate phenomena. The postulated double displacement mechanism for ATP phosphoribosyltransferase (EC 2.4.2.17) must be modified to account for the product stereochem.

IT 56475-05-9

RL: PROC (Process)
(optical rotation of)

RN 56475-05-9 HCAPLUS

CN Triphosphoric acid, P-[2-[1-[6-[[1-[1-formyl-2-(phosphonoxy)ethoxy]-2-oxoethyl]amino]-9H-purin-9-yl]-2-oxoethoxy]-3-oxopropyl] ester, stereoisomer (9CI) (CA INDEX NAME)



L14 ANSWER 228 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1975:439358 Document No. 83:39358 Effect of 9-(omega'-hydroxyalkyl)adenines and their triphosphates on the ATP-[32P]-pyrophosphate exchange reaction catalyzed by tryptophanyl tRNA synthetase. Prasolov, V. S.; Kritsyn, A. M.; Mikhailov, S. N.; Florent'ev, V. L. (Inst. Mol. Biol., Moscow, USSR). Dokl. Akad. Nauk SSSR, 221(5), 1226-8 [Biochem] (Russian) 1975. CODEN: DANKAS.

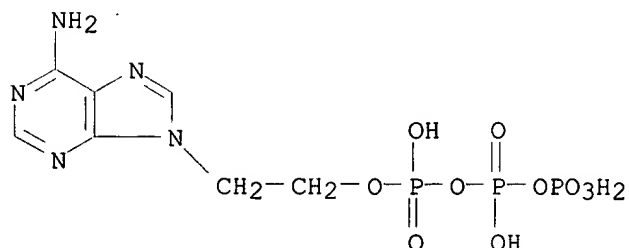
AB The response was studied of the title reaction catalyzed by the enzyme from bovine pancreas to adenine and adenosine and their 9-hydroxyalkylated analogs and their triphosphates and ATP with a 3'-O-Me block. Adenine and adenosine and their hydroxyalkyl analogs and triphosphates were competitive inhibitors of ATP in the pyrophosphate exchange reaction. Adenosine had inhibitory activity similar to that of ATP; the others were an order of magnitude less effective. Introducing a 2nd OH into the alkyl chain lowered the activity to that of adenosine itself. Tests of S- and racemic forms of the 9-(2,3-dihydroxypropyl)adenine showed that the configuration at the 2'-C is immaterial for binding the inhibitor to the active site. Inhibition by 3'-O-Me-ATP was noncompetitive. The ATPase mol. may have sites other than the ATP-binding site which interact with adenosine nucleotides. Evidence was found for esp. high activity of the 3'-OH group for ATP binding to the active site.

IT 55881-00-0 55881-01-1 55881-02-2

RL: BIOL (Biological study)
(tryptophanyl-tRNA synthetase response to)

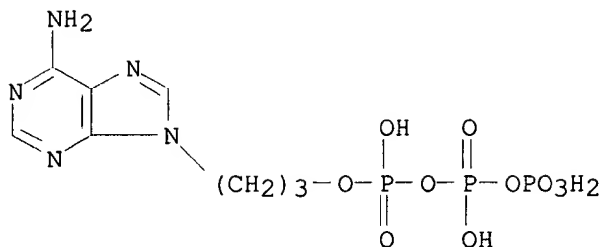
RN 55881-00-0 HCAPLUS

CN Triphosphoric acid, P-[2-(6-amino-9H-purin-9-yl)ethyl] ester (9CI) (CA INDEX NAME)

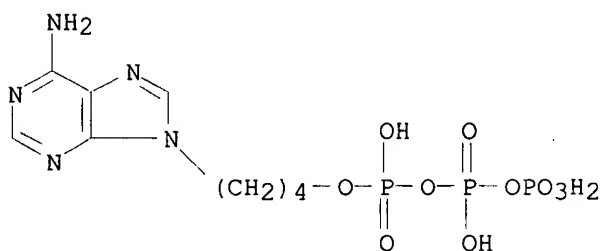


RN 55881-01-1 HCAPLUS

CN Triphosphoric acid, P-[3-(6-amino-9H-purin-9-yl)propyl] ester (9CI) (CA INDEX NAME)



RN 55881-02-2 HCAPLUS
 CN Triphosphoric acid, P-[4-(6-amino-9H-purin-9-yl)butyl] ester (9CI) (CA INDEX NAME)

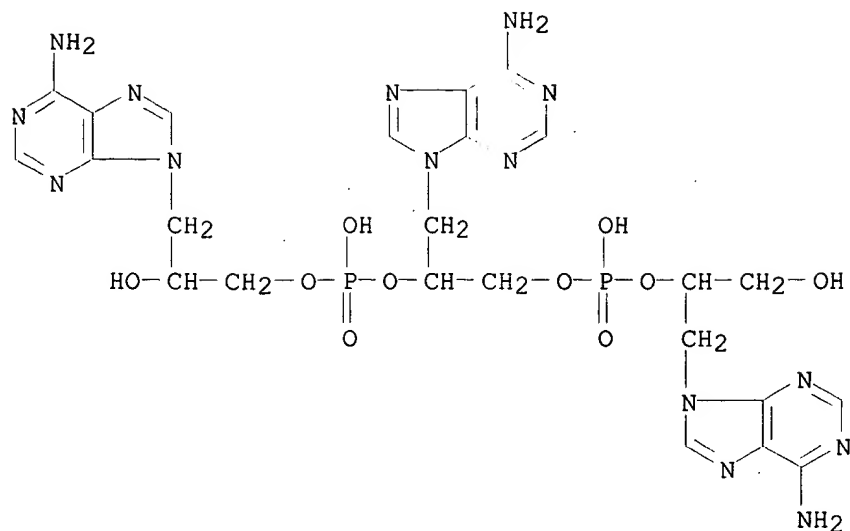


L14 ANSWER 229 OF 233 HCAPLUS COPYRIGHT 2002 ACS
 1975:171341 Document No. 82:171341 Nucleic acid components and their analogs. CLXXII. Aliphatic analogs of nucleosides, nucleotides, and oligonucleotides. Holy, A. (Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, Czech.). Collect. Czech. Chem. Commun., 40(1), 187-214 (English) 1975. CODEN: CCCCCA.

AB Condensation of thymine Na salt (I) with 1-O-p-toluenesulfonyl-2,3-O-isopropylidene-D-glycerol in DMF at 100.degree. and hydrolysis in refluxing 80% aq. AcOH gave a mixt. of (S)-1-(2,3-dihydroxypropyl)thymine and (S)-3-(2,3-dihydroxypropyl)thymine. The corresponding (R) enantiomers were prepd. by condensation of I with Me 5-O-p-toluenesulfonyl-2,3-O-isopropylidene-D-ribofuranoside, removal of the Me2C: group, NaIO4 oxidn., and NaBH4 redn. (RS)-1-(3,4-Dihydroxybutyl)thymine was prepd. from 1,2-O-isopropylidene-4-p-toluenesulfonyl-1,2,4-butanetriol. Condensation of N6,O2'-Diacetyl-(S)-(2,3-dihydroxypropyl)adenine 3'-phosphate with 3'-O-triphenylmethyl-(S)-9-(2,3-dihydroxypropyl)adenine and deblocking gave the ApA analog, (S)-9-(2,3-dihydroxypropyl)adenine-2'-phosphoryl-3'-(S)-9-(2,3-dihydroxypropyl)adenine. Repetition of this process gave the ApApA analog (S)-9-(2,3-dihydroxypropyl)adenine-2'-phosphoryl-3'-(S)-9-(2,3-dihydroxypropyl)-adenine-2'-phosphoryl-3'-(S)-9-(2,3-dihydroxypropyl)adenine (II). (S)-9-(2,3-Dihydroxypropyl)adenine-2'-O-phosphoryl-5'-adenosine and adenylyl-3'-yl-3-(S)-9-(2,3-dihydroxypropyl)adenine were also prepd. II and analogs of GpUpU, GpCpU, and GpApA triplets did not stimulate the aminoacyl-tRNA bond to ribosomes.

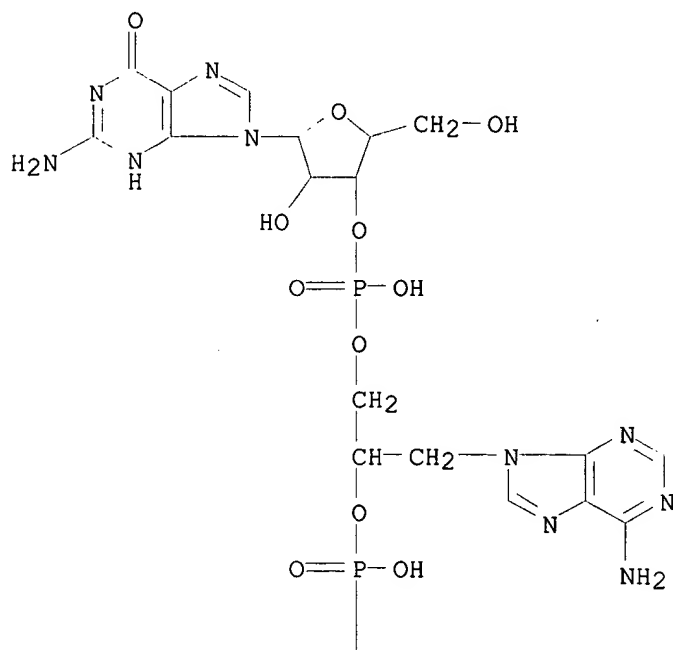
IT 55559-89-2P 55559-96-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)

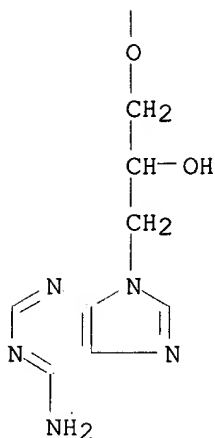
RN 55559-89-2 HCAPLUS
 CN Phosphoric acid, mono[3-(6-amino-9H-purin-9-yl)-2-[[[3-(6-amino-9H-purin-9-yl)-2-hydroxypropoxy]hydroxyphosphinyl]oxy]propyl] mono[2-(6-amino-9H-purin-9-yl)-1-(hydroxymethyl)ethyl] ester, stereoisomer (9CI) (CA INDEX NAME)



RN 55559-96-1 HCAPLUS
 CN 3'-Guanylic acid, mono[3-(6-amino-9H-purin-9-yl)-2-[[[3-(6-amino-9H-purin-9-yl)-2-hydroxypropoxy]hydroxyphosphinyl]oxy]propyl] ester, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

PAGE 1-A





L14 ANSWER 230 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1975:151215 Document No. 82:151215 Studies on mammalian ribonucleotide reductase inhibition by pyridoxal phosphate and the dialdehyde derivatives of adenosine, adenosine 5'-monophosphate, and adenosine 5'-triphosphate. Cory, Joseph G.; Mansell, Mary M. (Coll. Med., Univ. South Florida, Tampa, Fla., USA). Cancer Res., 35(2), 390-6 (English) 1975. CODEN: CNREA8.

AB Ribonucleotide reductase activity in a partially purified enzyme prepn. from Ehrlich tumor cells was irreversibly inhibited by the periodate oxidized (PI) derivs. of adenosine, AMP, and ATP, where the 2',3'-OH groups were oxidized to yield dialdehyde derivs. The NaBH4-reduced deriv. of PI-adenosine did not inhibit the reductase activity. Pyridoxal phosphate (I) reversibly inhibited ribonucleotide reductase; however, pyridoxal, pyridoxamine phosphate, pyridoxamine, and pyridoxine were not inhibitors. The addn. of NaBH4 to the enzyme-I mixt., followed by Sephadex G-25 chromatog., resulted in a protein fraction which had little reductase activity remaining. Inhibition by I was not influenced by increasing substrate concn. (ADP or CDP), but was decreased by increasing the concn. ratio of allosteric effector to I. Addn. of ADP to the enzyme-I mixt., which was then treated with NaBH4, partially prevented inhibition by I. Heat treatment of the reductase prepn. in the presence of I protected the enzyme against loss of ADP and CDP reductase activities. It appears that PI-adenosine, PI-AMP, and PI-ATP interact with the catalytic site, possibly forming Schiff bases between the aldehyde groups and the .epsilon.-NH2 group of lysine, and that I interacts with the regulatory site.

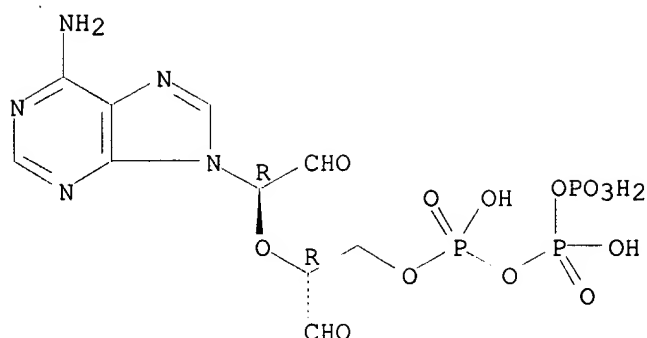
IT 54970-91-1

RL: BIOL (Biological study)
(ribonucleotide reductase inhibition by)

RN 54970-91-1 HCAPLUS

CN Triphosphoric acid, P-[(2R)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 231 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1973:432239 Document No. 79:32239 Interactions of the nonfunctional coenzyme binding site in dehydrogenases with [nicotinamide-ribofuranosyl]-[.omega.-(adenin-9-yl)-n-alkyl] pyrophosphates. Jeck, Reinhard; Wilhelm, Gabriele (Chem.-Physiol. Inst., Univ. Frankfurt, Frankfurt/M., Ger.). Justus Liebigs Ann. Chem. (3), 531-43 (German) 1973. CODEN: JLACBF.

GI For diagram(s), see printed CA Issue.

AB The NAD analogs I (n = 2-5) were prep'd. by condensation of .omega.-(adenin-9-yl)alkyl pyrophosphate with NMN. I and their enzymically prep'd. dihydro derivs. (II) had nearly identical chem. and phys. properties with NAD⁺ and NADH, resp. I and II were active as H acceptors or H donors, resp., with alc. dehydrogenase (E.C. 1.1.1.1) (III) from yeast or horse liver, lactate dehydrogenase (E.C. 1.1.1.27), or cytoplasmic or mitochondrial malate dehydrogenase (E.C. 1.1.1.37). I and II showed high Michaelis consts. compared to NAD⁺ and NADH, but lower (except with III of horse liver) catalytic consts.

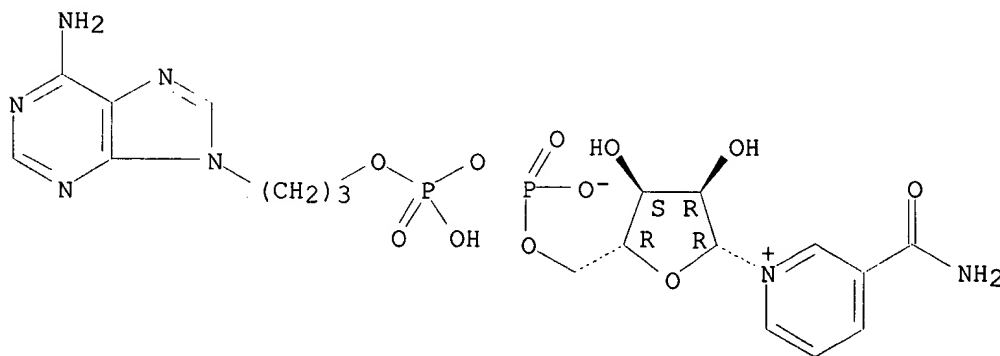
IT 42188-23-8P 42188-24-9P 42188-25-0P
42188-26-1P 42188-27-2P 42188-28-3P
42188-29-4P 42248-41-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 42188-23-8 HCAPLUS

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[7-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahept-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



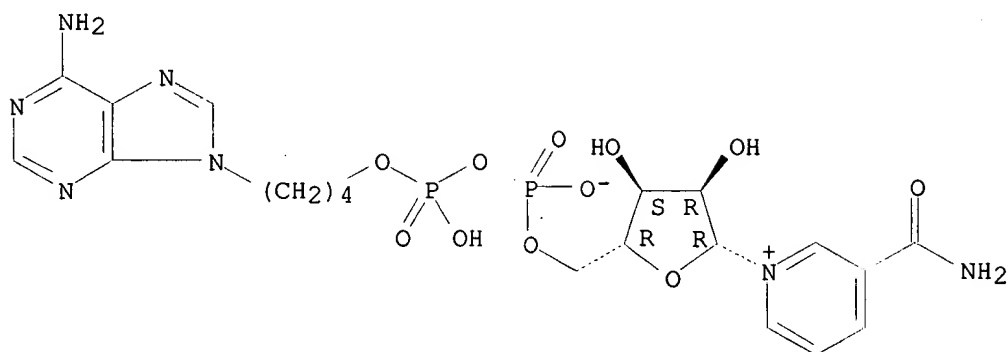
RN 42188-24-9 HCAPLUS

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[8-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphaoct-1-yl]-.beta.-D-

Searched by: Mary Hale 308-4258 CM-1 12D16

ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

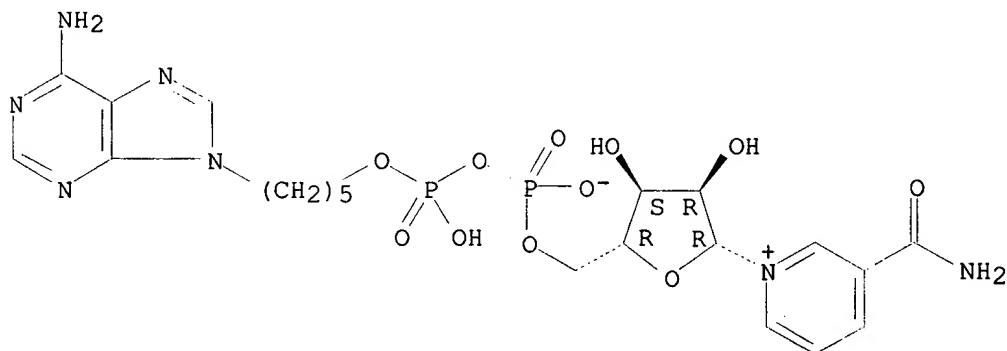
Absolute stereochemistry.



RN 42188-25-0 HCAPLUS

CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[9-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphanon-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

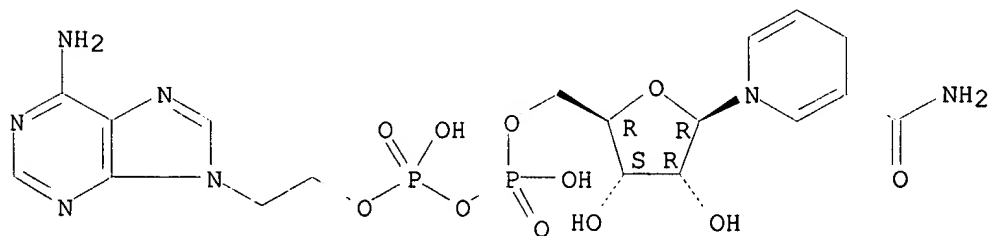
Absolute stereochemistry.



RN 42188-26-1 HCAPLUS

CN 3-Pyridinecarboxamide, 1-[5-O-[6-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahex-1-yl]-.beta.-D-ribofuranosyl]-1,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



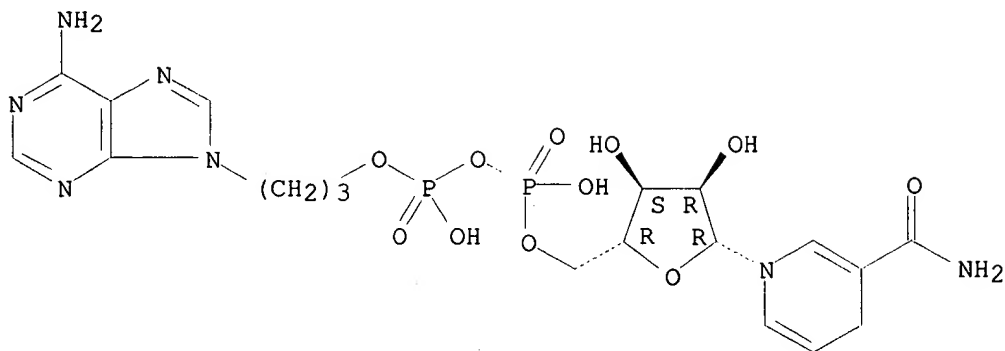
RN 42188-27-2 HCAPLUS

CN 3-Pyridinecarboxamide, 1-[5-O-[7-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahept-1-yl]-.beta.-D-ribofuranosyl]-1,4-

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dihydro- (9CI) (CA INDEX NAME)

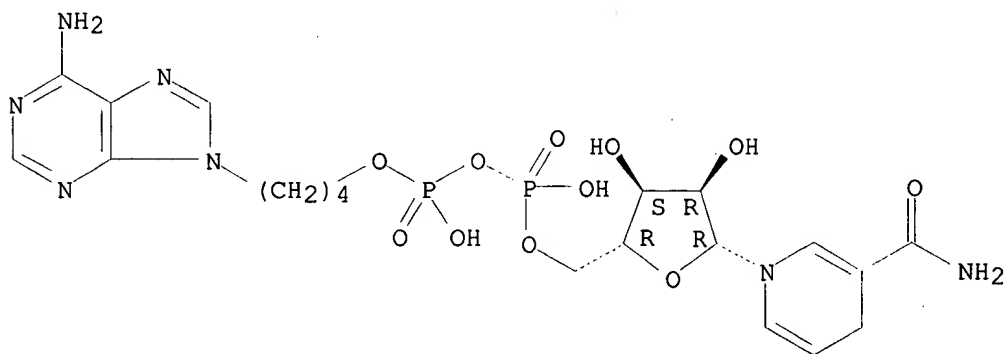
Absolute stereochemistry.



RN 42188-28-3 HCAPLUS

CN 3-Pyridinecarboxamide, 1-[5-O-[8-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphaoct-1-yl]-.beta.-D-ribofuranosyl]-1,4-dihydro- (9CI) (CA INDEX NAME)

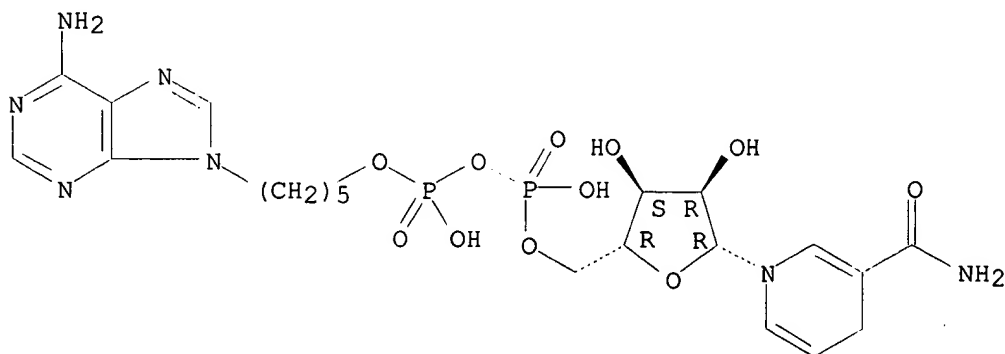
Absolute stereochemistry.



RN 42188-29-4 HCAPLUS

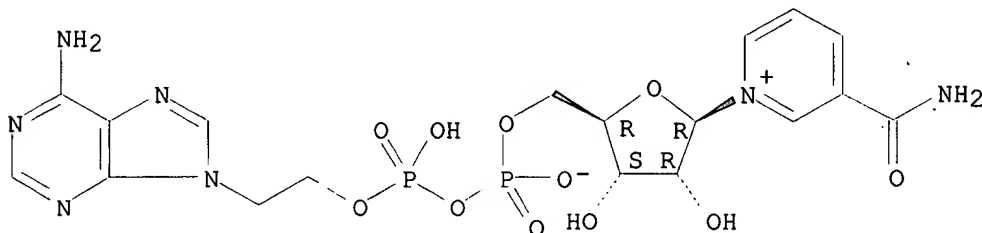
CN 3-Pyridinecarboxamide, 1-[5-O-[9-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphanon-1-yl]-.beta.-D-ribofuranosyl]-1,4-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



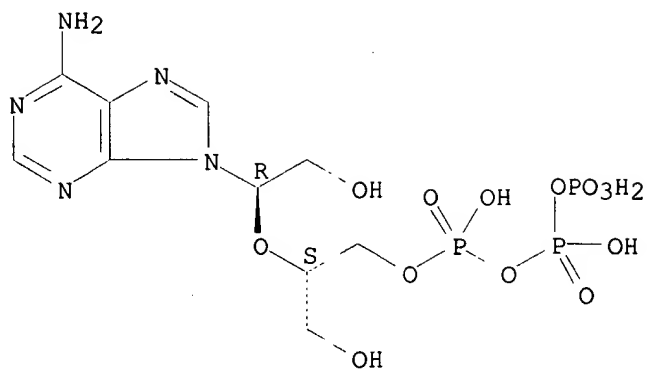
RN 42248-41-9 HCAPLUS
 CN Pyridinium, 3-(aminocarbonyl)-1-[5-O-[6-(6-amino-9H-purin-9-yl)-1,3-dihydroxy-1,3-dioxido-2,4-dioxo-1,3-diphosphahex-1-yl]-.beta.-D-ribofuranosyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 232 OF 233 HCAPLUS COPYRIGHT 2002 ACS
 1972:69233 Document No. 76:69233 Substrate properties of yeast tRNAPhe oxidized and reduced at the 3'-terminal ribose. Von der Haar, Friedrich; Schlimme, Eckhard; Gomez-Guillen, Manuel; Cramer, Friedrich (Abt. Chem., Max-Planck-Inst. Exp. Med., Goettingen, Ger.). Eur. J. Biochem., 24(2), 296-302 (English) 1971. CODEN: EJBICAI.
 AB Native yeast tRNAPhe and this tRNAPhe with the 3'-terminal AMP removed were oxidized by NaIO4 and subsequently reduced by NaBH4. The following investigations were undertaken with these substrates: aminoacylation in borate buffer and measurement of the lifetime of the aminoacylated oxidized and reduced tRNA, hydrolysis with snake-venom phosphodiesterase and pyrophosphorolysis with tRNA nucleotidyl transferase. Whereas the oxidized and reduced yeast tRNAPhe is a good substrate for the enzymes investigated, the corresponding tRNAPhe with the 3'-terminal AMP removed is a very poor, if any, substrate in these reactions. From the data obtained and from PMR investigations with oxidized and reduced AMP and ATP, it is concluded that the removal of the C2'-C3' bond and introduction of 2 H atoms instead distorts the original ribose conformation at the 3'-terminus. Under the assumption that this distortion is different for C75 and A76, the difference in reactivity between the 2 oxidized and reduced tRNAs can be explained.
 IT 35677-98-6
 RL: PRP (Properties)
 (conformation of)
 RN 35677-98-6 HCAPLUS
 CN Triphosphoric acid, P-[(2S)-2-[(1R)-1-(6-amino-9H-purin-9-yl)-2-hydroxyethoxy]-3-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 233 OF 233 HCAPLUS COPYRIGHT 2002 ACS

1968:497105 Document No. 69:97105 .alpha.-L-(9-AdeninyI)-.alpha.'-D-(hydroxymethyl) diglycolaldehyde phosphate esters. Alburn, Harvey E.; Dvovich, William (American Home Products Corp.). U.S. US 3395148 19680730, 3 pp. Continuation-in-part of U.S. 3317535 (English). CODEN: USXXAM. APPLICATION: US 19670306.

GI For diagram(s), see printed CA Issue.

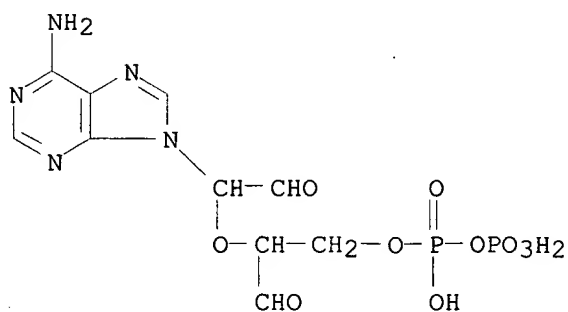
AB Diglycolic aldehyde phosphates (I), with antiinflammatory activity, are prepd. by the periodic acid oxidn. of adenosine mono-, di- and triphosphates, and diphosphopyridine nucleotide. Thus, 14.2 g. 5'-adenylic acid was oxidized with 450 ml. 0.1M periodic acid 1 hr. at 25.degree. in the dark. Then, 69 ml. of the soln. was passed over a Dowex-1-acetate column and the column washed with 3 vols. of H2O. The self-eluate and wash were freeze-dried to yield 8.5 g. I (R = H, n = 1). Similarly prepd. were I (R, n given) H, 2; H, 3; A, 2.

IT 21134-34-9P 21134-35-0P 21134-36-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

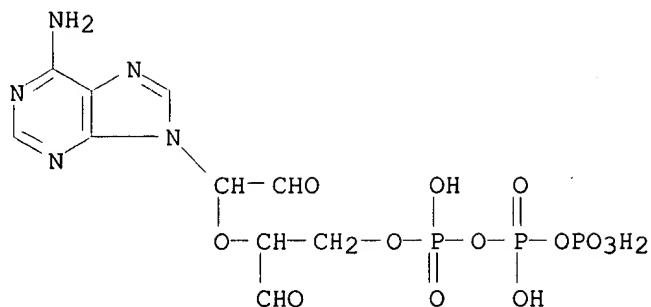
RN 21134-34-9 HCAPLUS

CN Diphosphoric acid, mono[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)



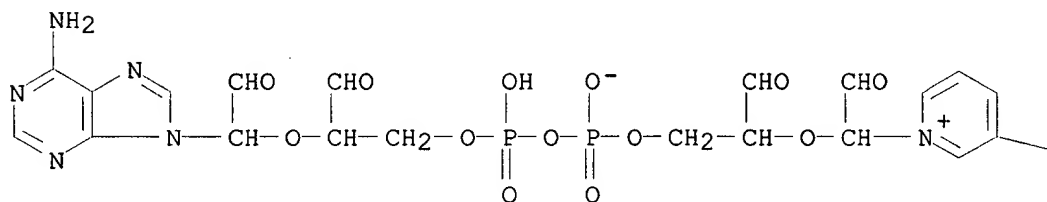
RN 21134-35-0 HCAPLUS

CN Triphosphoric acid, P-[2-[1-(6-amino-9H-purin-9-yl)-2-oxoethoxy]-3-oxopropyl] ester (9CI) (CA INDEX NAME)

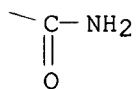


RN 21134-36-1 HCAPLUS
 CN Pyridinium, 3-carbamoyl-1-[formyl(1-formyl-2-hydroxyethoxy)methyl]-, trihydrogen pyrophosphate (ester), hydroxide, inner salt, monoester with 6-amino-.alpha.-(1-formyl-2-hydroxyethoxy)-9H-purine-9-acetaldehyde (8CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



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| | ENTRY | SESSION |
| FULL ESTIMATED COST | 294.47 | 1091.09 |
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<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> fil caol;s l13 or l14

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|--|------------------|---------------|
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| CA SUBSCRIBER PRICE | 0.00 | -132.37 |

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L15 4 L13
4 L13
4 L13 OR L14

=> d 1-4

L15 ANSWER 1 OF 4 CAOLD COPYRIGHT 2002 ACS
AN CA60:10770c CAOLD
TI coenzyme analogs - (XVI) synthesis of 9-D-erythrityladenine and its phosphates
AU Ikehara, Morio; Ohtsuka, E.
TI coenzyme analogs - (XVII) synthesis of purine nucleosides by the condensation of chloropyrimidines with glucosylamine
AU Ikehara, Morio; Tada, H.
IT 1463-10-1 3180-75-4 3181-38-2 3181-39-3 3351-13-1 3624-38-2
6207-14-3 7284-11-9 35215-21-5 53171-22-5 62998-22-5 73366-98-0
93688-76-7 93764-26-2 94735-22-5 95843-65-5 98106-89-9 98300-76-6
99689-06-2 99786-22-8 99800-67-6 100336-19-4 100336-20-7
100624-75-7 103908-77-6 104181-36-4 105232-03-9 107628-78-4 107989-22-0

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L15 ANSWER 2 OF 4 CAOLD COPYRIGHT 2002 ACS
 AN CA60:7060a CAOLD
 TI interaction between synthetic adenosine triphosphate analogs and
 actomyosin systems - (II)
 AU Ikehara, Morio; Ohtsuka, E.; Kitagawa, S.; Tonomura, Y.
 IT 41591-26-8 89305-67-9 95140-33-3 **108267-43-2**

L15 ANSWER 3 OF 4 CAOLD COPYRIGHT 2002 ACS
 AN CA55:25964b CAOLD
 TI coenzyme analogs - (IX) synthesis of 6-alkylamino-9-.beta.-D-
 ribofuranosylpurine 5'-monophosphate
 AU Ikehara, Morio; Ohtsuka, E.; Ishikawa, F.
 IT 1867-73-8 2620-62-4 4566-77-2 19083-21-7 73237-86-2
98335-84-3 109047-65-6 110553-70-3 116977-26-5

L15 ANSWER 4 OF 4 CAOLD COPYRIGHT 2002 ACS
 AN CA55:25964a CAOLD
 TI coenzyme analogs - (VIII) synthesis of 6-amino-.beta.-purine-9-ethanol and
 its phosphates
 AU Ikehara, Morio; Ohtsuka, E.
 IT 707-99-3 1670-62-8 4551-95-5 6623-88-7 98197-64-9 98427-97-5
110475-69-9

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 for more information. See STNote 27, Searching Properties in the CAS
 Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -132.37 |

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